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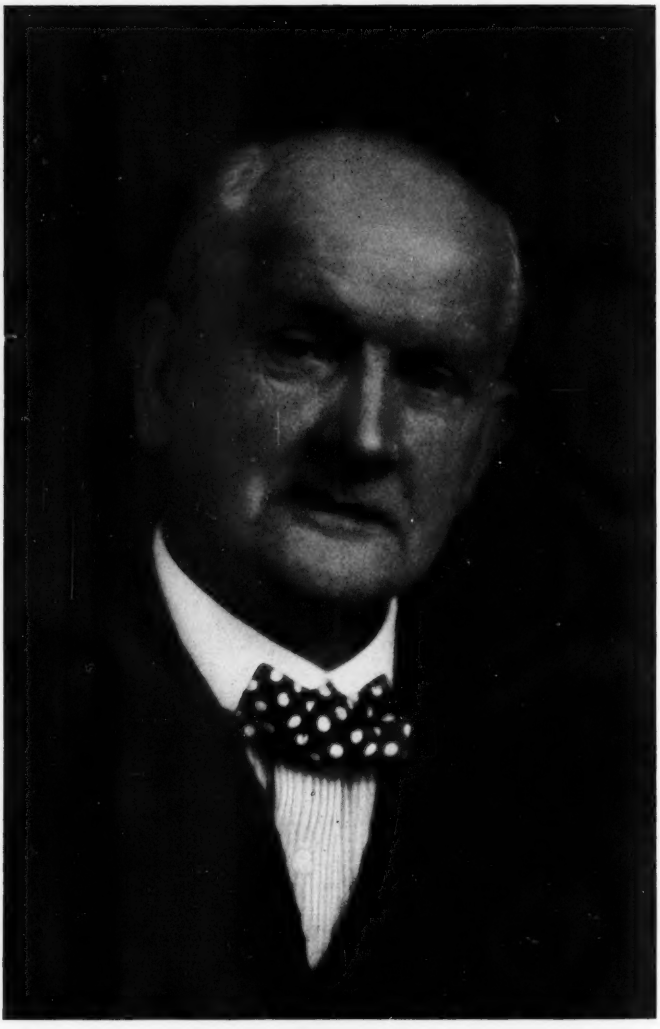

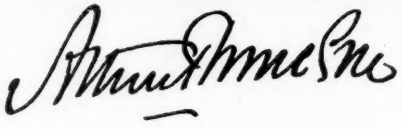

Photo by
A. H. Bodle, Oxford

ARTHUR THOMSON

(1858–1935)

M.B. (Edin.), M.A., Hon. D.Sc. (Oxford), Hon. LL.D. (Edin.), Hon. D.C.L. (Durham), F.R.C.S.

Lecturer in Human Anatomy, 1885; Professor, 1895–1933, in the University of Oxford; Student of Christ Church; Professor of Anatomy at the Royal Academy, 1900–1934; President of the Anatomical Society, 1906–1909

IN MEMORIAM

ARTHUR THOMSON, AS I KNEW HIM

I THINK that I saw him for the first time when the British Medical Association met in London in 1895. C. B. Lockwood and I were the Secretaries of the Anatomical Section and Arthur Thomson suggested a new way of plotting out the abdomen by means of triangles. I forget how it was done, but it was quite ingenious. Lockwood, in his caustic way, said that no sensible surgeon wanted the abdomen plotted out at all, but that the triangles with a little rearrangement might make an artistic ornament for a garden. Thomson was very angry indeed and accused Lockwood of frivolity and flippancy, sadly out of place, he said, in a scientific meeting; but the latter, who had just criticised another anatomist's exhibit by saying that it smelt more and showed less than any specimen he remembered, went on goading the poor little man until I thought that they would be enemies for life. When I blamed Lockwood later for his brutality he said that "Tommy" understood just as well as he did that the chief duty of a secretary was to bring a little life and sunshine into these otherwise drab meetings and that there was no need for any uneasiness on my part. He was quite right, for after lunch I found the two of them drinking coffee together and talking about boat sailing in the most friendly way in the world.

I have raked up this memory of long ago from my store because it is so characteristic of my two old friends. I can still see Arthur as he stood, that day, on the platform of the anatomical theatre at King's College, his boyish, clean-shaven face red with indignation at the quiet gibes of his critic. I can see the well-cut suit and the broad bow tie and hear the deep voice rolling out weighty words, each one marked by a slight nod of the head, for he had caught the solemn, emphatic manner of speaking of his old master, Sir William Turner, to the life.

My knowledge of Thomson in Oxford is slight, for I only saw him there when I went to examine his students, or to some scientific meeting, but I always stayed at his house at these times and I like to think that I had the friendship of his wife and two daughters as well as that of himself. In the evenings he always asked one or two friends in to meet me and I learnt to understand and to envy the ease with which Oxford dons can adapt themselves to all sorts and conditions of men and make them feel at home. I suppose that I have seen almost all the anatomical departments of the British Isles, and I know that many of them try to copy the one at Oxford, even though their heads want Arthur Thomson's artistic sense, and it seems to me that, in showing other anatomists how a department can be clean, light, fresh and

artistically planned, he has done more for anatomy than many of us fully grasp.

But it was in London that I saw most of him, and when the day's work at the London M.B. or one of the College of Surgeons' examinations was over we usually dined together at a restaurant or some club. The Athenaeum and the Savile were too like Oxford, he said, to give him the change he needed, but later, when I had exchanged the Savile for the Savage Club, he found what he wanted and thoroughly enjoyed the freedom from the conventions of polite society, and the absence, for a time, of all those formalities which interested me so much when I went to dine in Hall with him at Oxford. Thomson's own club was the "Arts" in Dover St, where he met all his artist friends, though one great drawback it had in that a man, who, so far as I know, was his only enemy, used it a good deal.

But I am writing for the *Journal of Anatomy* and hitherto have said hardly a word about Arthur Thomson as an anatomist. There is no doubt that he was thoroughly interested in his subject, but it was his profession and not his whole life. I fancy that in his earlier and more impressionable days in Edinburgh he came so much under the influence of Turner as to decide that what Turner was he would like to be.

I know well, I suppose that every teacher knows, the personal influence which the head of a department has upon clever boys of 17 or 18 who have just exchanged the rule of a professional pedagogue for that of a man who, like themselves, is still a student, though one who has added something to the world's knowledge. If the professor is a man of marked personality, his interests and lines of research become those of some of his students, and I think that Thomson became an anatomist because Turner was one; otherwise he would have been an artist by profession as he always was at heart. Still, he did a good deal of solid, painstaking research in anatomy and anthropology, such as the "Races of the Thebaid" and the "Earlier Stages of Embryology", but, since he did not care to advertise it in any way, it is known to comparatively few. Of course his book on *Anatomy for Art Students* comes under a different heading, for it is a text-book, duly brought before the world by his publishers, and will be well known and admired for many years to come.

About his own work and successes Thomson was always silent, perhaps too silent, though he was the most generous of men in his praise of good work by others. I think that he was quite content with the place which he had won in the scientific world, and that the quiet but undoubted influence which he could bring to bear was all that he wanted. Such honours and recognitions as came to him were none of his seeking, and I know that when the Royal Anthropological Institute offered him its Presidency he declined the honour because he knew his limitations, he said, and did not feel that he was fitted to take so important a post. The Presidency of the Anatomical Society was different. That, as the Professor of our oldest English University, he could not well refuse, and those of us who are old enough to have been anatomists in 1906 remember how well

he carried out his duties, just as he did those of the President of the Anatomical Section of the International Congress which met in London in 1913.

So great was his kindness of heart that sometimes it came near warping his judgment, and often, after a more than usually heavy day of rejections for the Primary F.R.C.S. Examination, I have known him quite depressed because he had not passed more candidates, though this was in spite of the fact that he was the most lenient and gentle examiner the board has known, and had we all been like him the diploma would have lost a great deal of its value.

I want to record his weak points, otherwise this personal appreciation would be unjust to him, and I suppose that the quickness with which he resented any apparent injustice or rudeness to himself or to others was too great for a man of really well-balanced judgment and hindered him thinking over the other side of the matter before he spoke or acted. Perhaps, too, he was too generous and warm-hearted for an ideal examiner, a job he always hated. Beyond that I can think of nothing to his discredit, try as I will.

And now that he is gone I feel that anatomy has lost a capable, honest, warm-hearted gentleman, and I, a very dear friend, but it gives me some pleasure to think that I should have been allowed to record these memories of a friendship of nearly forty years, a friendship over which no cloud ever cast its shadow.

F. G. Parsons.

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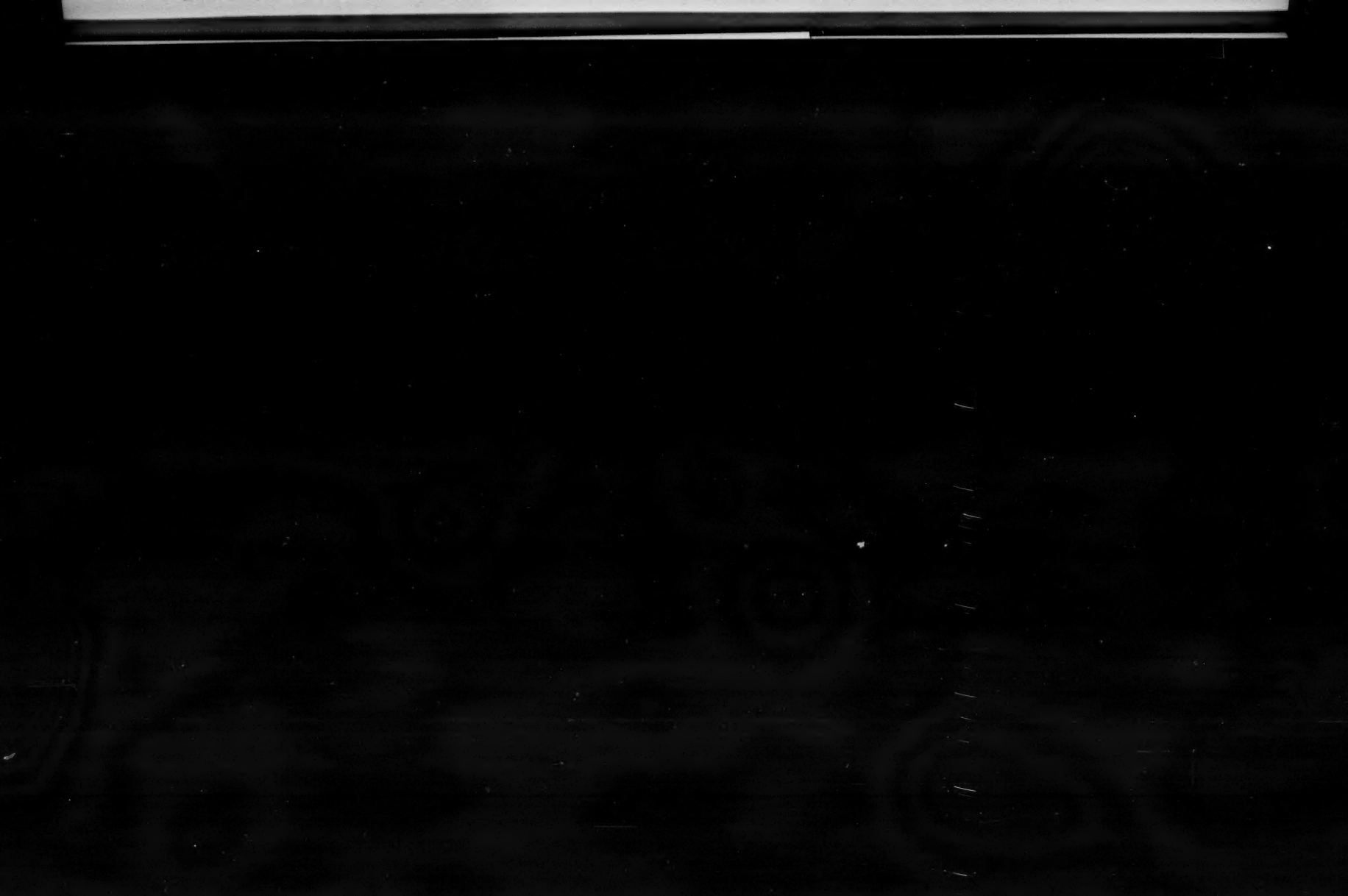

OBSERVATIONS ON THE CONDUCTING SYSTEM OF THE HEART[1]

By D. M. BLAIR and F. DAVIES

From the Hambleden Department of Anatomy, King's College, London

INTRODUCTION

The present work was begun with the object of investigating the nerve supply of the conducting system of the heart. At an early stage in the study it was found that the neurohistological technique which we employed for the purpose of displaying the nerve elements had the additional effect of revealing the detailed structure of the muscular elements of the system more clearly than the methods commonly used for that purpose. We therefore decided to attempt a complete survey of the structure and nervous connections of the cardiac conducting system, in the hope of amplifying previous work and clearing up existing discrepancies. To begin with, attention was specially directed to the human heart, because of its clinical importance, and to the bovine heart, as providing in some ways a useful comparison and because its conducting system, richly supplied with nerves, seemed particularly suitable as an initial subject for neurohistological study. The present paper records the observations so far made in these two forms on the sinu-atrial and atrio-ventricular nodes, the atrio-ventricular bundle and its two limbs, together with their immediate neural connections. In the following text the two types of heart are dealt with concurrently, to avoid repetition; but we are careful to indicate whether statements are applicable to both types or only to one of them.

MATERIAL

All the bovine material was obtained from adult animals immediately after death. The human material comprised three hearts removed at post-mortem examination, one from a subject aged 14 years, 6 hours after death, one from a child aged 9 months, 12 hours after death, and one from a child aged 10 months, 12 hours after death.

The sinu-atrial region of the human and bovine hearts was studied in blocks cut out of the whole thickness of the heart wall so as to include more than the upper half of the sulcus terminalis, and the adjacent parts of the right atrial and sinus walls and the entry of the superior vena cava. These were sectioned, some at right angles to the sulcus terminalis, others parallel to it.

The specialised atrio-ventricular connections in the human heart were examined in blocks which included the adjacent parts of the interatrial and

[1] Published with the aid of a grant from the Johnson Symington Memorial Bequest.

interventricular septa, the entry of the coronary sinus, and the region beyond (in front of) the pars membranacea septi. These blocks were sectioned parallel to the coronary sulcus. In the bovine heart, the atrio-ventricular node and its prolongations, together with the atrio-ventricular bundle and its two limbs, with some of the adjacent myocardium, were dissected out carefully with the aid of binocular magnifiers in the fresh heart, transferred immediately to the fixing fluid, and ultimately cut longitudinally. Further, in the bovine heart, tangential sections (parallel to the endocardial surface) were cut of blocks which included the atrio-ventricular node and proximal part of the atrio-ventricular bundle.

The blocks from both the sinu-atrial and atrio-ventricular regions in both types of heart were deliberately cut out in such a manner that they extended on all aspects well beyond the sites customarily ascribed to the specialised conducting system in these regions in the hearts of placental Mammals. All preparations were cut into serial sections 10 μ thick.

TECHNIQUE

A histological method was required which would give reasonably consistent results and be applicable to the high-power study of serial sections of fairly large blocks. To begin with, preliminary trial was made on cardiac material of numerous neurohistological methods, using silver nitrate, gold chloride, osmic acid or methylene blue. The special merit of silver impregnation in differentiating the muscular elements of the conducting system became early apparent and led us to concentrate on such methods.

In view of the remarks of Woollard in favour of methylene blue rather than silver technique, in his paper on the innervation of the heart (1926), we may be permitted to point out some reasons for the contrary view. The intravital methylene-blue technique cannot be practised on the human heart, and neither that nor the supravital method can be made to produce complete nerve differentiation throughout a comparatively thick block of tissue such as must be used in studying the conducting system in a large heart. Even when small pieces of tissue are used, it is difficult to make sure of precise nerve-muscle relationships without high-power study of thin serial sections, and we are convinced that the preparation of paraffin sections of methylene-blue material causes appreciable loss of staining.

Of all the silver methods tried, that of Ranson (1914) seemed likely to give good results most readily in comparatively large blocks. The undoubted excellence of Bielschowsky preparations, when successful, is offset by the notorious difficulty of the method, and by its limitation to very small blocks. One great drawback of Ranson's method, at any rate when applied to muscular tissues, is the amount of shrinkage and friable hardening produced owing to fixation in what is almost absolute alcohol. We found, however, that fixation in 10 per cent. neutral formalin, followed by 10 per cent. formalin with 5 per cent. of ammonia added, instead of the ammonia-alcohol fixation of the

original technique, obviated these undesirable effects and greatly improved the differentiation of the nerve and muscle fibres. The former were revealed with a clarity and fineness equalled only in the best Bielschowsky results, but much more readily and if necessary in large blocks, while the muscle fibres were rendered more translucent and their striations became much more clearly visible than when using the unmodified Ranson technique. Variations were tried out in every stage of the technique; in this experimental work we were much helped by suggestions from Dr E. W. McClelland, Lecturer in Chemistry, and Dr W. Robson, Reader in Biochemistry, of King's College; and Dr E. E. Hewer, Reader in Histology at the London School of Medicine for Women, was good enough to discuss with us various modifications in the light of her own experience of the Ranson technique (1933). What we came to adopt as our standard method is indicated in the following statement, where the times are those actually employed in the preparation of one of our most successful specimens:

1. Formalin 10 per cent. (4 per cent. formaldehyde), neutralised with ammonia	10 days
2. Formalin 10 per cent., 95 c.c. Ammonia fortis, 5 c.c. }	48 hours
3. Running tap water	48 hours
4. Distilled water (many changes)	3 hours
5. Pyridine	24 hours
6. Distilled water (many changes)	4 days
7. Silver nitrate 2 per cent. in incubator at 35° C.	4 days
8. Distilled water (many changes)	3 hours
9. Pyrogallic acid, 4 g. Formalin 5 per cent., 100 c.c. }	24 hours
10. Distilled water (changed)	1 hour
11. Transfer to 50 per cent. alcohol, dehydrate, clear in benzol or chloroform, and embed in paraffin wax.	

Stages 7–10 are carried out in the dark.

The following notes are numbered to correspond with the stages in the process given above:

1. Neutralisation (to litmus) with ammonia is distinctly beneficial. Longer fixation does no harm. To give the best results, material must be fixed immediately after death; hence none of our human preparations has been quite so successfully impregnated as those of animal hearts.

2. This improves the differentiation of both nerve and muscle fibres and renders nuclei more visible; less or more ammonia is disadvantageous. This solution is *not* a fixative (hence must be preceded by 1), because in this strength the formalin is completely converted into hexamine (hexamethylenetetramine) by the ammonia, and any formic acid in the formalin into ammonium formate. An aqueous solution of hexamine and ammonium formate chemically equivalent to the theoretical product of the formalin-ammonia combination gives results

nearly but not quite so good as the formalin-ammonia solution; a solution of hexamine alone was still less good.

3. To remove formalin completely and to save distilled water.

4. Tap water distilled once over potassium permanganate in an all-glass still which has been in use for several years, so that no soluble material remains in the glass.

5. Longer in pyridine is undesirable, as the tissue becomes brittle and the neural impregnation is not so good.

6. Pyridine must be thoroughly removed; continue for 24 hours after all odour of pyridine has disappeared.

7. Longer in silver nitrate results in poorer impregnation of nerve fibres.

8. Less washing causes deposit.

9. Longer reduction disadvantageous. Several other reducing agents were tried without advantage.

10. Prolonged washing with distilled water is unnecessary as pyrogallic acid comes out still more readily in the alcohols, but the 90 per cent. alcohol should be changed until it remains colourless.

SINU-ATRIAL NODE

The sinu-atrial node of the heart of Man and other placental Mammals was originally described by Keith and Flack in 1907 as a mass of peculiar muscle fibres, some nerve cells and nerve fibres, embedded in the densely packed connective tissue which surrounds the artery or arterial circle that lies at the junction of sinus and right atrium. The fibrous tissue in which the nodal fibres are embedded is considered by these authors to belong to the epicardium and to correspond to the infolded epicardial fibrous tissue in the right venous valve at the sinu-atrial junction of the lower vertebrate heart. Further, these authors note that in the human heart the nodal fibres are cross-striated, fusiform, arranged in a plexiform manner and related mainly to the sulcus terminalis in the region of the entry of the superior vena cava. Many subsequent investigators have verified the main features of this description, though Tandler (1913), Koch (1922), Zimmermann (1923) and Monckeberg (1924) could not establish with certainty the transverse striations of the nodal fibres. Bruni (1924) illustrates cross-striation of the nodal fibres in the calf, and Burian (1925) gives a convincing description and illustrations (drawings) of cross-striation in the nodal fibres of the human heart, in material stained for the purpose with iron haematoxylin after fixation in Heidenhain's "Susa" mixture. Walmsley in 1929, although he refers to Burian's work, summarises the position with the statement that transverse striation of the sinu-atrial nodal fibres (in the human heart) has not been certainly demonstrated. Wingate Todd and van der Stricht in 1919, and Wingate Todd in 1928, from their study of the adult human heart, maintain that both nodes (sinu-atrial and atrio-ventricular) are non-specialised parts of, and structurally identical with, the general cardiac Purkinje system.

In the present work we have observed that the sinu-atrial node is more extensive than existing descriptions imply. In both human and bovine hearts the sinu-atrial node consists of a main mass lying in relation to the upper part of the sulcus terminalis, and of tapering extensions, both above and below the main mass, which pass beyond the scope of our blocks. The upper extension passes in front of and above the entry of the superior vena cava into the right atrium, so that *in situ* the sinu-atrial node would have a horseshoe shape, the entry of the superior vena cava lying below and behind the concavity of the horseshoe. Bruni (1924) has described a similar arrangement of the node in Ruminants, and Pace (1924) in the sheep. Segre (1926) has also described this arrangement in Man and further notes that the intermediate portion of specialised fibres connecting the two limbs of the horseshoe does not develop until after birth. The lower tapering extension of the node, as stated above, passes beyond the scope of our blocks, and therefore must extend downwards beyond the middle of the sulcus terminalis.

The main nodal mass, moreover, extends through the entire thickness of the heart wall, spreading from the subepicardial to the subendocardial connective tissue (Plate I, figs. 1–4); as it approaches the endocardium it spreads out so that in sections at right angles to the sulcus terminalis it appears wedge-shaped, with the base of the wedge towards the endocardium (Plate I, fig. 1). This does not seem to have been appreciated previously. In this situation the nodal fibres, together with the enveloping connective tissue, intervene between the sinus musculature (covered with a thick endocardial layer) and the atrial musculature (covered with a thin endocardium). Elsewhere the sinus and atrial musculature are continuous. The main mass of the node thus lies immediately on the sinus side of the crista terminalis, and, except where it impinges on the subendocardial or subepicardial connective tissue, it is directly contiguous all round with the adjacent atrial or sinus muscle. In the human heart the main nodal mass extends from the subepicardial connective tissue to the endocardium both behind (i.e. on the sinus side) and in front (i.e. on the atrial side) of the base of the crista terminalis.

The nodal fibres in both human and bovine hearts are spindle-shaped and branched, and are set rather loosely in the surrounding connective tissue (Plate III, fig. 9, and Plate V, fig. 17). For the most part they are arranged with their long axes parallel with the long axis of the sulcus terminalis, so that in sections at right angles to the sulcus they are cut almost transversely. In such sections, however, many of the fibres, particularly those near the epicardium and those near the atrial myocardium, are cut very obliquely or even longitudinally. The nodal fibres immediately adjacent to the main artery and its branches which, as all previous workers have noted, run along in the axis of the sulcus terminalis and embedded in the node, are arranged in a circular or spiral fashion around the artery (Plate I, fig. 2, and Plate II, fig. 5). In the bovine heart the majority of the fibres of the sinu-atrial node (with the technique employed) are about 9 μ in their widest diameter, with a common range

of from 3 to 17 μ. In the human heart (14 years old) the majority of the nodal fibres are about 5 μ wide, with a common range of from 2 to 7 μ. With the silver technique employed in the present work the nodal fibres are seen to be distinctly striated transversely (Plate III, fig. 9, and Plate V, fig. 17), the smaller fibres, which comprise the greater proportion, being striated throughout their entire thickness, while the larger fibres have an appreciable perinuclear unstriated zone, and thus resemble in structure (though not in size) some of the "typical" Purkinje fibres found in the bovine heart beneath the ventricular endocardium, or in the atrio-ventricular bundle and its two limbs. Each nodal fibre has a nucleus which is round or oval in shape and centrally situated; in some fibres two nuclei are present, close to one another in the centre of the fibre. The structural features of the nodal fibres revealed by silver impregnation leave no doubt as to the essential muscular nature of the sinu-atrial node.

With regard to the relation of the nodal fibres to the neighbouring myocardial fibres, Walmsley (1929) states that direct continuity of nodal and atrial muscle fibres (in the human heart) has not been established, but that there is no definite boundary of the node; its fibro-muscular tissue gradually fades into the surrounding myocardium. Wakefield and Chandler (1924) could not find any evidence of direct continuity of nodal and myocardial fibres in the adult human heart; they state that a delicate connective tissue sheath intervenes between the nodal and atrial muscle fibres; their sections, incidentally, were cut at a thickness of 25 μ. Shaner (1929), on the other hand, found evidence of direct continuity of the sinu-atrial nodal fibres with both sinus and atrial muscle in the heart of the foetal calf.

In the present work the peripheral nodal fibres of both human and bovine hearts were frequently seen to become directly continuous with the atrial or sinus fibres, either by end-to-end union, or by union through one or more side processes of the nodal fibres (Plate IV, fig. 14). One nodal fibre may thus become directly continuous with two or more atrial or sinus myocardial fibres. With a Zeiss binocular microscope and the highest power apochromatic lenses and aplanatic condenser, no interruption of continuity by any sheath formation or otherwise could be made out at the junctional zone; the nodal fibre passes directly over into the myocardial fibre in both bovine and human hearts. In places, at the periphery of the sinu-atrial node, it was difficult to say where nodal fibres ended and myocardial fibres began. This was particularly the case where the peripheral nodal fibres were of medium size and completely cross-striated so that they closely resembled the neighbouring myocardium in appearance. The precise site of continuity was most readily observed between the larger nodal fibres in the ox heart and the neighbouring myocardial fibres.

Another type of continuity was observed in the bovine heart. Subepicardial nodal fibres extend caudally in a subepicardial plane and become directly continuous with much larger fibres which have exactly the same

appearance as the large subendocardial ventricular Purkinje fibres in the same heart. These large atrial Purkinje fibres, in their turn, were traced caudally for a short distance and passed into direct continuity with the subepicardial atrial muscle fibres, joining these on their epicardial aspect (Plate IV, figs. 15 and 16). This observation is of interest in relation to the much discussed question of the presence or absence of "typical" large Purkinje fibres in the atria of placental Mammals. One of the present writers (Davies, 1931) has reviewed the literature on this question in a previous paper in this *Journal*. Various authors have described collections of Purkinje fibres in the right atrium of Man and other placental Mammals, but it is noteworthy that the situations in which they have been found differ with the investigators, and moreover the atrial Purkinje fibres appear, from the descriptions of these workers, to form isolated collections, unconnected with either the sinu-atrial or the atrio-ventricular node. In the avian heart one of us (Davies, 1930) observed that the rich abundance of atrial Purkinje fibres was continuous on the one hand with the sinu-atrial node, and on the other with the ordinary atrial muscle, but no specialised connection between the sinu-atrial and atrio-ventricular conducting systems could be made out; the atrio-ventricular nodal fibres became directly continuous only with the atrial myocardium. So far as the present work goes the bovine heart offers a parallel picture, namely, some of the sinu-atrial nodal fibres are continuous with large "typical" Purkinje fibres, which, in their turn, are continuous with the atrial myocardium, as described above, while, as mentioned later in this paper, the atrio-ventricular nodal fibres become directly continuous with the atrial myocardium without the intervention of large "typical" Purkinje fibres.

In the human heart the difficulty arises of recognition of the various types of fibres in the conducting system. With the silver technique used in the present study, the sinu-atrial nodal fibres are plainly seen to exhibit transverse striation (Plate III, fig. 9). Moreover, the breadth of the nodal fibres (human, aged 14 years) varies from 2 to 7 μ, while that of the atrial muscle in the same heart ranges from 5 to 11 μ (Plate IV, fig. 13). Hence many of the nodal fibres are as large as the atrial muscle fibres, and while the small nodal fibres or even the larger ones which exhibit only peripheral transverse striation are easily recognisable, the nodal fibres of intermediate size that show marked and almost complete transverse striation are only with difficulty distinguished from myocardial fibres. This difficulty must be borne in mind in assessing references in the literature to scattered collections of Purkinje fibres in the atria. After the examination of much material and bearing in mind our findings in the bovine and other hearts, we have come to the conclusion that continuity with undoubted specialised muscle is the criterion which best determines the nature of a doubtful muscle fibre. In our blocks from the right atrium of the human heart we have found no large "typical" Purkinje fibres such as are seen in the bovine heart; neither are such found in the human atrio-ventricular bundle, as will be shown later.

A further relation of the sinu-atrial nodal fibres, not hitherto described, was observed in the present investigation. As mentioned above, the nodal fibres in the vicinity of the nodal artery and its branches are arranged in a circular manner around these vessels (Plate I, fig. 2, and Plate II, fig. 5). In numerous places some of these peri-arterial nodal fibres turn into the arterial wall and become contiguous with the unstriped muscle fibres of the media. In the bovine heart some of these long, slender, cross-striated nodal fibres are seen actually to pass into the arterial tunica media and become directly continuous with the plain muscle fibres (Plate II, fig. 6). The presence of a distinctly cross-striated muscle fibre in the middle of the tunica media of an artery provided a very striking and unusual picture. In the human heart, while numerous peri-arterial nodal fibres pass into immediate contiguity with the outer surface of the arterial tunica media (Plate II, fig. 7), we could not with absolute certainty make out any penetration into the media, although the nodal fibres appeared to blend with the outermost plain muscle fibres of the arterial coat.

In both types of heart there is no nodal vein in the sense of a vena comitans of the nodal artery, but a number of small veins (venae cordis minimae) drain from the nodal tissue into the cavity of the right atrium. This agrees with the description of Géraudel (1928). We have seen no special relation between nodal fibres and the nodal venules.

In the endocardial connective tissue in the immediate neighbourhood of the sinu-atrial node in both types of heart, we have observed unstriated muscle fibres of ordinary visceral type. Such have been described in various situations in the endocardium, although no complete account of their arrangement and topographical distribution in any species has been given. They form a thick layer on the sinus side of the crista terminalis, but only a very thin layer on the atrial side of the crista. Near the sinu-atrial node we observed long tapering tongues of ordinary atrial muscle fibres which run into the endocardium and appear to become continuous with these endocardial unstriated muscle fibres (Plate II, fig. 8). We could, however, trace no direct connection between the sinu-atrial nodal fibres and these visceral muscle fibres, a thick layer of endocardial connective tissue intervening between the two. We hope to investigate further the topography of this endocardial plain muscle with particular reference to its possible relationship to the conducting system.

The question of direct connection between the sinu-atrial and atrio-ventricular nodes by means of specialised muscle is discussed at the end of the section dealing with the atrio-ventricular node.

The penetration of sinu-atrial nodal tissue from epicardium to endocardium, and its extent beyond the customarily recognised limits of this specialised structure, as above described, are of interest in relation to the experimental work that has been done on this region of the heart. For example, Hering (quoted by Lewis, 1925) claimed that, after isolation of the sinu-atrial and atrio-ventricular nodes from the mass of the right atrial tissue, the right atrium

continued to beat, and concluded that there are other atrial centres capable of rhythmic action. These hearts, however, were subsequently examined by Koch, who found nodal tissue attached to the remaining mass of atrial tissue, and, as Lewis asserts, this emphasises the importance of strict histological controls in experiments of this type. Furthermore, Lewis has shown that to cool the "head" of the sinu-atrial node in dogs is insufficient to induce atrio-ventricular rhythm. The present work further emphasises the difficulty of experimental removal of the entire sinu-atrial node, and as any nodal tissue remaining will be capable of initiating atrial contraction, throws open to still more serious question the validity of previous experimental work as a basis for the supposition of other (ectopic) centres with the same rhythmic powers as the node.

ATRIO-VENTRICULAR NODE

In both bovine and human hearts the arrangement of the atrio-ventricular nodal tissue has a characteristic appearance quite distinctive from that of the ordinary atrial myocardium or of the sinu-atrial node. In the bovine heart the atrio-ventricular nodal fibres form a loose spongework of muscular trabeculae, with the meshes occupied by loose connective tissue and abundant capillary blood vessels (Plate V, fig. 18). The spongework is much more compact in the human atrio-ventricular node, with less connective tissue between the nodal fibres (Plate III, fig. 10). In both types the trabeculae branch and anastomose with each other, and are not orientated in any particular plane. The individual nodal fibres are cylindrical in shape and branch like ordinary cardiac muscle. Walmsley (1929) states that, at the best, transverse striation of the fibres of the atrio-ventricular node (in the human heart) is necessarily insignificant. With the silver technique employed in the present investigation the nodal fibres in both human and bovine hearts are seen to be distinctly cross-striated (Plate III, fig. 10, and Plate V, fig. 18). For the most part the striation extends throughout the fibres, except for a narrow perinuclear clear zone. Each nodal fibre contains one or sometimes two centrally situated round or oval nuclei. As stated above for the sinu-atrial node, the appearance revealed by the silver method leaves no doubt as to the muscular nature of the atrio-ventricular node.

In the human heart (aged 14 years) the nodal fibres vary commonly from 3 to 11 μ in breadth, with the majority about 7 μ. The bovine nodal fibres are rather larger, mostly about 10 μ in breadth, with a common variation from 3 to 14 μ. In both human and bovine hearts, the atrio-ventricular nodal fibres differ from those of the sinu-atrial node in that they are shorter, rather thicker, more cylindrical and more branched than the sinu-atrial nodal fibres, which are commonly of elongated fusiform type. We do not agree with the observations of Shaner (1929), who, while noting that the sinu-atrial and atrio-ventricular nodes in the adult bovine heart are not especially alike in structure, states that the clear-cut cell walls or membranes of the atrio-ventricular node are absent in the sinu-atrial node, and that the sinu-atrial node forms a diffuse branching

meshwork that does not resemble anything found in the atrio-ventricular node. The differences between the sinu-atrial and atrio-ventricular nodes that we have observed comprise those of the arrangement, shape and size of the constituent muscle fibres as stated above. Our observation that the fibres of the sinu-atrial node are in general rather smaller than those of the atrio-ventricular node may be of importance in relation to the correlation, expressed by Lewis as the law of cardiac muscle, between the size (thickness) of a cardiac muscle fibre and its rate of conduction, rhythmicity, length of systole and glycogen content; the fibre size, glycogen content and rate of conduction increase in the following order: nodal, ventricular, atrial, Purkinje; while the length of systole and rhythmicity diminish in the same order.[1] The smaller size of the sinu-atrial nodal fibre noted in the present work might have a bearing on any difference that may be found to exist in the rhythmicity of the sinu-atrial and atrio-ventricular nodes, which difference might be correlated with the onset of the wave of excitation for cardiac contraction at the sinu-atrial node (the pacemaker, Lewis).

Dissections of the atrio-ventricular node in the fresh bovine heart were made with the aid of binocular magnifiers. Atrial prolongations of the main nodal mass as described and figured by Curran (1903) were made out. The entire dissected mass, including the atrio-ventricular node and its prolongations, was subjected to histological section (after treatment with the silver technique), which revealed that the prolongations consisted of nodal fibres which after a very short course became directly continuous with the ordinary atrial myocardium. One of these prolongations extended towards the opening of the coronary sinus, others upwards in the atrial septum to become continuous with the right and left atrial muscle components of the septum. These atrial septal prolongations did not extend, as Curran states, almost as far as the superior vena cava, but after a very short course the nodal fibres comprising them became directly continuous with the atrial myocardium. In the human heart a large prolongation from the atrio-ventricular node to the left atrial muscle component of the atrial septum was seen piercing the upper part of the trigonum fibrosum dextrum in its upward and backward course. Further, in the human heart (14 years old) an extension of the nodal tissue was traced for a short distance into the anterior wall of the left atrium, where it became continuous with the atrial myocardium. In its course it passed upwards and to the left, immediately behind the basal attachment of the right posterior (non-coronary) cusp of the aortic valve. This nodal prolongation appears to us to correspond in position to at least a part of the interatrial node described by Shaner (1929) in the early foetal calf heart. Shaner, however, observed that

[1] Our preparations of the adult bovine heart show that the order of fibre size in the ox is the same as that given by Lewis in the dog, which is here referred to. But in our preparations of human heart (aged 14 years) the order is different; the thickness of fibre increases in the order: nodal, atrial, atrio-ventricular bundle, ventricular. (Compare figs. 9, 10, 13, 11 and 12, which are all from the same human heart, aged 14 years, and of the same magnification.)

the interatrial node had no connection with the atrio-ventricular node, and, in the calf at least, disappeared in the later stages of foetal life, gradually fading into ordinary atrial muscle.

No "typical" Purkinje fibres were seen in the immediate vicinity of the atrio-ventricular node in either atrial wall in either the human or the bovine heart; the nodal fibres become directly continuous with the atrial myocardium. In both the human and the bovine heart the change from nodal to atrial myocardial fibres is a very gradual one, in contrast with the sudden change in character from atrio-ventricular nodal fibres to large "typical" Purkinje fibres at the beginning of the atrio-ventricular bundle in the bovine heart, as described below. It is difficult, if not impossible, to say exactly where nodal fibres end and atrial muscle begins. Branching of both nodal and atrial muscle fibres occurs in the territory of junction, and the fibres, both atrial and nodal, vary so much in diameter that it is often difficult to assign any one fibre to node or atrial muscle with certainty. The network formation of the nodal fibres is continued up to the junctional territory; in the junctional zone the network formation is rather less marked, but the parallel arrangement of very slender fibres at the upper part of the atrio-ventricular node, described by Cohn (1909) as the atrio-nodal junction, was not observed by us in either the bovine or human heart.

The prolongation from the atrio-ventricular node towards the ventricular septum described by Curran (1903) in the calf heart was also noted by us in the dissected heart of the ox. In the human heart we traced this prolongation in the serial sections to the base of the septal cusp of the tricuspid valve, but no direct continuity of these nodal fibres with the myocardium of the ventricular septum could be made out, connective tissue, continuous with the trigonum fibrosum dextrum, intervening in all sections between nodal and ventricular muscle. Holmes (1921) came to the same conclusion from his study of the hearts of the sheep and ox. In this region, however, we observed continuity between these nodal fibres and the myocardium of the right atrium which descends for a short distance into the base of the septal cusp of the tricuspid valve. Further, we noted in this region of the human heart no direct continuity between the myocardial fibres of the right atrium and those of the ventricular septum, although in a few sections the terminal fibres of the ventricular septum and right atrium approached very close to each other. This was one of the regions of the heart where Kent (1893) noted direct continuity between the myocardial fibres of the right atrium and those of the ventricular septum in the hearts of the rat and young rabbit and to a lesser extent in the guinea-pig and hedgehog. In the monkey, only very few fibres were found by Kent to establish atrio-ventricular continuity, and these were described as transversely striated, branched, spindle-shaped cells, intermediate in character between ordinary heart muscle and unstriped muscle, with long tapering ends extending almost completely through the atrio-ventricular fibrous ring from atrium to ventricle and establishing muscular continuity between atrium and ventricle.

Similar fibres were seen in the present work in the human heart in the fibrous tissue between the right atrium and the ventricular septum, beneath the base of the septal cusp of the tricuspid valve, but they appear to us to be of the nature of the "insertions" of the cardiac muscle fibres (atrial and ventricular) into the right fibrous ring. Pace (1924), who studied these fibres carefully, believed likewise and referred to them as "fibres terminales spéciales". We certainly could not find in the human heart evidence of direct continuity by means of these fibres between the right atrium and the ventricular septum. In this connection it may be remarked that Lewis states that the physiological evidence is strongly opposed to the idea of the fibres described by Kent taking part in conducting impulses from atrium to ventricle.

The sinu-atrial node, as stated above, extended beyond the scope of our blocks, but the atrio-ventricular node appeared to be entirely contained within the blocks of tissue removed in both human and bovine hearts. The atrial extensions of the atrio-ventricular node were all traceable into continuity with atrial myocardium. Recently Tudor Jones (1932) has described direct continuity between the sinu-atrial node and the atrio-ventricular node in the 24 mm. human embryo, the connection lying in the base of the right venous valve. Previously Thorel (1906), in his study of adult human hearts (over 40 years of age), found a direct connection between the sinu-atrial and atrio-ventricular nodes consisting of fibres of Purkinje type, but subsequent investigators have failed to corroborate this. While we would defer final opinion on this question until we have studied sections of entire hearts, our present study reveals no indication of such a connection in the post-natal heart. It may be that the connection described by Tudor Jones in the embryonic heart is of a temporary nature, and, if confirmed, would obviously be important from the point of view of the development of the nodes and their embryological and phylogenetic relation to one another. On the other hand, Shaner (1929) found that, while the atrio-ventricular node appeared in the 9 mm. calf embryo, the sinu-atrial node did not appear until the 100 mm. stage, and he does not describe any direct connection between the two.

ATRIO-VENTRICULAR BUNDLE

In the bovine heart the atrio-ventricular bundle arises from the centre of the main mass of the atrio-ventricular node, as the shaft fits into the knob of a walking stick (Plate VI, fig. 20). In the proximal part of the atrio-ventricular bundle, as it leaves the atrio-ventricular node, the specialised muscle fibres are arranged in plexiform strands with a general direction in the long axis of the bundle (Plate V, fig. 19, and Plate VI, fig. 22); subsequently the bundle fibres form parallel longitudinal fasciculi. From the very commencement of the bundle the fibres stand out clearly from either the nodal or ordinary myocardial fibres because of their relatively enormous size, about 30 μ in average diameter. Commonly two, three or more fibres of the atrio-ventricular node become uninterruptedly continued into one Purkinje fibre, joining the latter end on or

on its side; the transversely striated myofibrillae of the nodal fibres can be clearly seen to pass into the Purkinje fibre to become continuous with the transversely striated portions of the Purkinje fibre (Plate VI, fig. 23). There is no sign of any sort of septum across the junction of nodal and Purkinje fibres, and frequently the continuity provides the striking appearance of a thin nodal fibre suddenly swelling out into a broad bundle fibre. It is not easy to determine the exact configuration of these bundle fibres. But it seems to us that descriptions, such as those of Wingate Todd (1928), are mistakenly based on deceptive appearances seen in oblique sections. The fluted column fibre form suggested by these descriptions, we consider to be an erroneous impression of a fasciculus of several individual fibres lying very close together, or of sections at the side-to-side junctions of individual Purkinje fibres. The fibres in a fasciculus are continuous with one another by branches split off longitudinally in regions where a slight interval occurs between the fibres, or by localised areas of side-to-side union where they are more compactly arranged. The fasciculi themselves fork and join with one another; this is more obvious in the proximal, plexiform part of the bundle. In the distal part of the bundle and in the limbs, long lengths of cylindrical fibres without any side connections can be traced in longitudinal sections of the dissected specimen. In these elongated cylindrical fibres numerous small rounded nuclei are seen, mostly placed immediately below the surface of the fibre, exactly as in skeletal muscle (Plate VII, fig. 26). Multiple central nuclei, however, are commoner, particularly in the shorter fibres. The fibres are definitely cross-striated; this striation may be indistinct or absent in localised areas within the fibre, but the cross-striation is not confined to the periphery, and the central part of the fibre is not entirely unstriated. In other words, in these large "typical" Purkinje fibres the transversely striated longitudinal myofibrillae are irregularly distributed in the fibre and do not completely fill it as they do in ordinary cardiac muscle (Plate VI, fig. 23, and Plate VII, fig. 26).

In the human heart the fibres at the beginning of the atrio-ventricular bundle differ very little in histological structure from those of the atrio-ventricular node. Holmes (1921) has likewise commented on the absence of clear distinction between the node and the beginning of the bundle. The fibres in the proximal part of the bundle are slightly larger than the atrio-ventricular nodal fibres, averaging about 9μ in diameter as against 7μ for the nodal fibres, and have a less ragged appearance because they branch less markedly. When running parallel in the more distal part of the bundle and in the proximal parts of its right and left limbs, the fibres closely resemble the ordinary ventricular muscle fibres; the latter are slightly larger with an average diameter of about 12μ (Plate III, figs. 11 and 12). Only a small proportion of the bundle fibres exceed this size. Most of the fibres in the bundle and in the proximal parts of its right and left limbs present transverse striation throughout their thickness (Plate III, fig. 11, and Plate VII, fig. 25), with the exception of a narrow, clear, central, perinuclear zone, and thus resemble the

neighbouring ventricular myocardial fibres. The few larger fibres bear some resemblance to "typical" Purkinje fibres in respect of irregular and incomplete transverse striation, but even these only slightly exceed the ventricular muscle fibres in size. In some of the bundle fibres two centrally situated rounded or oval nuclei are found. The elongated peripherally nucleated Purkinje fibres observed in the bovine heart are not seen in the human bundle; indeed in the bundle fibres in the human heart there is no room for nuclei elsewhere than in the centre of the small fibres. Holmes (1921) has previously noted these relative sizes of the bundle fibres and ventricular muscle fibres in the human heart, but gives no actual measurements. The bundle and its limbs are surrounded with a delicate connective tissue sheath, which in places is so thin as hardly to be recognised at all. In these places, particularly in the proximal part of the right limb, where the limb fibres closely resemble the neighbouring myocardial fibres, the limb itself is recognised histologically in isolated transverse sections only with some difficulty. The thinness and delicate nature of the sheath, as Holmes has also observed, explain the difficulty or impossibility of injection (e.g. with Indian ink) in the human heart, rupture and extravasation through the sheath taking place immediately it is exposed to even a slight pressure. Such was the experience, also, of Aagaard and Hall (1915).

NERVE CELLS IN RELATION TO THE CONDUCTING SYSTEM

We hope later to make a complete topographical survey of the intracardiac ganglia by means of serial sections of entire hearts, but the following observations on the present material may be recorded. Groups of nerve cells are placed in the immediate neighbourhood of the sinu-atrial node in both ox and man; they are more numerous in the ox. For the most part they are situated on the epicardial aspect of the node, where in both types of heart some of the groups of nerve cells lie in juxtaposition with the superficial nodal fibres. We found no nerve cells in the interior of the sinu-atrial node in either type of heart; neither did Meiklejohn (1913) in the heart of the monkey (*Callitrix*) or of Man. Fahr (1910), on the other hand, occasionally found nerve cells in the sinu-atrial node of the human heart. Groups of nerve cells were also found close to the atrio-ventricular node in both forms, in the lower and back part of the atrial septum, mostly placed in the connective tissue between the right and left atrial muscle components of the septum. Here again nerve cells are more numerous in the bovine heart, where a few small groups of cells were found buried within the atrio-ventricular node, an observation previously made by Fahr (1910). In the bovine heart, small groups of nerve cells were found in relation to the atrio-ventricular bundle and the proximal parts of its right and left limbs, some immediately adjacent to the surface of the bundle and its limbs, some amidst the Purkinje fibres (Plate VI, fig. 21, and Plate VIII, figs. 28 and 29). In the human heart, however, we observed no nerve cells within the atrio-ventricular node, or in the course of the atrio-ventricular bundle or

its right or left limb. Fahr (1910) and Holmes (1921) also failed to find nerve cells in these situations in the human heart. Wilson (1909) has described nerve cells in the atrio-ventricular bundle and its two limbs in the calf, sheep and pig, and Meiklejohn (1913) in the left limb of the atrio-ventricular bundle in the guinea-pig. Woollard (1926) states that intracardiac ganglia in the dog, cat, rabbit and guinea-pig (but compare findings of Meiklejohn mentioned above) are limited caudally by the coronary sulcus. Perman (1924) and Francillon (1928) failed to find subepicardial ganglia caudal to the coronary sulcus in the human heart. But, in the bovine heart, as stated above, nerve cells are present in both limbs of the atrio-ventricular bundle. Further, sections of the entire calf heart impregnated with silver are in the process of preparation, and a preliminary survey of those already cut has revealed numerous ganglia in the epicardium more than half way down the ventricles.

We noticed that the silver technique we employed tended to differentiate the nerve cells found in relation to the conducting system into two types: a generally larger type of rounded form and very finely stippled texture, which assumed a pale yellow colour, and a smaller type of somewhat angular form, which stained more densely with a deep brown or almost black coloration which prevented any study of the internal texture of the cell body. Often the small, darkly staining cells showed branching dendrites. Both types of cell were to be seen in most collections of nerve cells in the heart. This recalled the histological differentiation of ganglion cell types described by Kiss (1932) on the basis of his prolonged osmic acid method of staining. Prof. Kiss himself was good enough to examine some of our specimens and agreed that the cell types we observed corresponded to those described by him. Further, Bacsich (1933), a colleague of Kiss, using the prolonged osmic acid technique has found these types of nerve cells in the coronary plexus and in the posterior wall of the right atrium of the pig. Although we draw attention to the similarity of the two types of nerve cells noted by us to those described by Kiss in ganglia elsewhere, we are at present unable to offer any views on any possible functional significance which this morphological difference may imply. We tried the experiment of photographing these nerve cells with infra-red sensitive plates (1933*a*) and found that the pale cells appeared as seen by the eye under the microscope, but the dark cells revealed a coarsely granular texture not otherwise visible (Plate VIII, figs. 30 and 31). Careful study of the infra-red photomicrographs and of enlargements of them showed that this "granularity" was of a reticular nature. Bacsich (1932) has analysed the coloration of the dark nerve cells by the osmic acid method of Kiss as being due to the presence of coarse lipoidal granules within the cells. It may be that the darkly staining reticulum observed in the dark cells with the silver technique and infra-red photography corresponds to a neurofibrillary network in the meshes of which lie the lipoidal granules stained by the osmic acid method.

Intricate terminal arborisations of nerve fibres could be made out in connection with some of the cells in the cardiac ganglia. But to trace precise

relationship, or lack of relationship between the nerve cells and the nerve fibres is very difficult if not impossible.

NERVE FIBRES IN RELATION TO THE CONDUCTING SYSTEM

All parts of the bovine conducting system were found to be profusely supplied with nerve fibres; in the human heart the nerves are much fewer but are not inconsiderable. The contrast was least in the sinu-atrial node and greatest in the atrio-ventricular bundle and its limbs. In both sinu-atrial and atrio-ventricular nodes in the bovine heart there is an abundance of fine nerve bundles or isolated nerve fibres twining amidst the nodal fibres; in the sinu-atrial node the nerves appear in part at any rate to be related to the ganglia in the vicinity, while in the case of the atrio-ventricular node large nerve trunks, connected with the adjacent ganglia, sweep forward in the lower part of the atrial septum to the node. The human sinu-atrial node is well supplied with nerve fibres, the atrio-ventricular node less so. The atrio-ventricular bundle and its right and left limbs in the bovine heart are so richly supplied with nerves—large fasciculi, finer pencils and isolated fibres—that they might truly be called neuromuscular bundles (Plate VI, fig. 21). On the other hand, the nerves in the human atrio-ventricular bundle and its limbs are much fewer and do not form large fasciculi, but run in very small bundles, or, more commonly, as individual fibres between the muscle fibres. Cohn (1909), using iron haematoxylin and van Gieson's stain, failed to find any nerves in the region of the atrio-ventricular node or bundle in monkeys. Meiklejohn (1913), however, noted a nerve supply to the atrio-ventricular bundle in the monkey (*Callitrix*) much finer than in Ungulates, but found only a few small nerve fibres in the human atrio-ventricular bundle. Wilson (1909) found abundant nerves in the atrio-ventricular bundle and its limbs in the calf, sheep and pig.

All the nerve fibres seen in the conducting system in both types of heart appear to be unmyelinated; in the large nerve bundles associated with the ganglia close to the sinu-atrial node, however, some myelinated fibres were seen. It must be remembered, however, that with silver impregnation it is difficult to distinguish between unmyelinated and finely myelinated fibres, particularly in longitudinal section.

A detailed search was made for possible nerve endings in the conducting system muscle, in particular for intra-protoplasmic endings such as described, for example, by Boeke (1932), Woollard (1926) and Tudor Jones (1927) in the ordinary myocardium, and by Boeke (1932) in the muscle fibres of the atrio-ventricular bundle. But the most careful study has failed to reveal in our specimens any such ending within a muscle fibre of the conducting system. This is, of course, no positive proof that such do not exist. But our technique, in our best preparations, did reveal intra-protoplasmic nerve endings in the plain muscle fibres of the tunica media of branches of the coronary arteries in the bovine heart (1933*b*), so that we feel justified in placing some weight on

our negative findings in respect of the conducting system. In every case where at first sight a nerve fibre seemed as if it might be penetrating a muscle fibre, we each of us made careful independent examination with a binocular microscope and in every case agreed that the nerve fibre did not penetrate into the striated portion of the muscle fibre. It is of interest to note that Woollard, in his remarks made when our present work was communicated to the Anatomical Society of Great Britain and Ireland, then stated that his general impression was that the nerve endings were invariably pericellular in position (*J. Anat.*, Lond., 1933, vol. LXVIII, *Proc. Anat. Soc.*, p. 151).

It may be noted in this place that P. Stöhr, Jr. (1932) has been unable, after studying hundreds of specimens, to demonstrate any sign of nerve fibres within the muscular coat of arteries, and asserts that this agrees with the results of most authors. So far as the branches of the coronary arteries of the bovine heart are concerned, the present technique certainly demonstrates a rich muscular innervation of the media. We have also seen clearly the endings of these nerves in the form of a paranuclear loop (Plate VII, fig. 27) similar to that described in relation to the plain muscle of the ciliary body by Boeke (1932), and that of the gastro-intestinal tract by Lawrentjew (1926), Stöhr, Jr. (1932) and Hill (1927).

One complicating factor in studying the ultimate nerve-muscle relationships in the conducting system is that the capillary blood vessels in the system, themselves very plentiful and closely applied to the muscle fibres, are accompanied by fine nerve fibres. As the use of a pyridene bath in a silver technique tends to diminish the impregnation of capillary endothelium, great care must be taken to determine that a nerve fibre, suspected of ending in connection with a muscle fibre, is not really a capillary nerve. Our observations in respect of nerve endings have invariably been checked by examination with a Zeiss binocular microscope and one-twelfth inch apochromatic objective.

We find that ultimate nerve-muscle relationships in the conducting system of the bovine heart which can be considered as true nerve endings are of two quite different types. One of these has been described by several previous authors, and is readily seen in the atrio-ventricular bundle of the ox, where with our technique the large clear Purkinje fibres form a pale yellowish background against which it is easily seen. It takes the form of a network of extremely delicate nerve fibres wrapped round the Purkinje fibre and in immediate contact with it. The nerve fibres show no varicosities, nor are any nuclei seen in special relation to the network. Although clearly seen, this network may lie in relation to a small part only of a Purkinje fibre; in fact, long lengths of Purkinje fibres are devoid of any perifibrillar nerve network. A similar nerve network was observed in relation to the nodal fibres, both sinu-atrial and atrio-ventricular. We are satisfied that such a perifibrillar network is entirely on the surface of the muscle fibre (i.e. epilemmal) and sends no processes into the interior of the muscle fibre. Its arrangement suggests the possibility of afferent function.

The second type of nerve ending which we have made out, we suggest may be the true motor nerve ending of the bundle or nodal fibre (Plate VII, fig. 24). It is formed by a single unmyelinated nerve fibre, usually slightly beaded and finely varicose, which runs close alongside and parallel with the muscle fibre for some distance, and then ends in the centre of a group of rounded or oval nuclei. These nuclei are set in a yellow-coloured protoplasm which seems to be directly continuous with the cytoplasm of the muscle fibre, but the cross-striations of the muscle fibre do not extend into this nucleated zone. When such an ending is seen in profile in a longitudinal section, the nucleated zone appears as an elongated slight bulging on the side of the muscle fibre. Beyond this localised region, the straight edge of the muscle fibre has a definite limiting "line" of slightly darker tint, which is not an optical effect only, but suggests the presence of a definite sarcolemma. In the region of the bulging, this sarcolemma cannot be identified, so that it is difficult to trace the exact boundary of the pale-stained nucleated mass on its free surface; but since it seems to be directly continuous deeply with the cytoplasm of the muscle fibre, it is presumably hypolemmal in nature. We could not observe, however, any evidence of penetration of branches of the nerve into the muscle fibre to become continuous with the cross-striations as Tudor Jones (1927) has described in the case of the ordinary cardiac muscle. Within the clear cytoplasm of the bulging zone, the nerve takes a slightly angulated course amidst the nuclei and shows slight branching by means of very short side processes at the angulations. No trace was seen of a periterminal network as described by Boeke. The whole structure recalls the motor end-plate of skeletal muscle; we would characterise it as a greatly elongated nerve ending of simple filiform type in a richly nucleated sole-plate. Our observation that some of the long Purkinje fibres have multiple nuclei disposed like those of skeletal muscle strengthens the possibility that the motor nerve endings in the two types of muscle may approximate in structural arrangement. Meiklejohn (1913) has described nerve fibres ending in relation to groups of nuclei, some of which she thinks may be muscle nuclei of the nodes or bundle. Undoubtedly some of these endings described and figured by her are endings in the connective tissue of the conducting system, such as we have ourselves noticed. But we think that others may be of the nature of sole-plates similar to those we have just described, although she does not clearly indicate the relationship to the muscle fibre cytoplasm.

In the human heart we could not find the fine perifibrillar network we observed in the bovine heart. This may be due to failure of impregnation of these very fine nerve fibres, as the freshest human material we used was obtained 6 hours post-mortem. But we have observed numerous extremely fine isolated nerve fibres twining amidst the muscle fibres of the conducting system and in intimate relation to their surface. Fresher material has recently been obtained for further study of this question. We did, however, observe in relation to the muscle fibres of the human atrio-ventricular bundle, single nerve

fibres running on the surface of a muscle fibre and, after becoming extremely fine, ending in a terminal knob apparently in a slight unstriated bulging of the surface of the muscle fibre (Plate VII, fig. 25). It resembled a diminutive arrangement of what we had observed in the bovine heart, but without the nest of nuclei, and may possibly be an even simpler type of motor nerve ending in the human heart. In relation to the coronary arteries in the human heart, we observed many nerve fibres penetrating the media, but, probably for the reason given above, we could not make out with certainty penetration of the nerve endings into the plain muscle fibres.

In both bovine and human hearts the capillary blood vessels were observed to be accompanied by nerve fibres, often in the form of a plexus. From these pericapillary plexuses nerve fibres were often seen to pass to the muscle fibres of the conducting system.

CONCLUDING REMARKS

Before concluding this paper we would like to refer to two points in connection with the use of the term Purkinje fibres with which we have been impressed by our study of the literature in conjunction with our own observations.

In the first place, the term Purkinje fibre has been used in different connections by different workers. On the one hand, it has been used to cover all the muscle fibres in the conducting system which itself is referred to as the Purkinje system. On the other hand, the term has been restricted to large muscle fibres such as are seen, for example, in the atrio-ventricular bundle of the ox, and which are specially characterised by the irregular and incomplete distribution within the fibre of cross-striated myofibrillae; in the present paper we have used in this sense the expression "typical" Purkinje fibres, and we think the use of the term Purkinje fibre should always be thus limited.

In the second place, in comparing our observations on the human and bovine conducting systems we have been struck by the marked difference in appearance of the muscle fibres in the atrio-ventricular bundles of these two types; the term "typical" Purkinje fibres would be applicable to the bovine bundle but not to the human, yet the two must be regarded as homologous. Therefore the term in its restricted use is not always applicable to corresponding parts of the conducting system in different types.

We think it important to call attention to these two points because if they are not kept in mind, reports of the presence or absence of Purkinje fibres in different parts of the heart may be misinterpreted. For example, a statement that no Purkinje fibres are present in the atria of a particular type of heart does not necessarily imply that no ramifications of the conducting system are present in those atria. We have already stressed our view that continuity with a known part of the conducting system, one or other of the nodes or the atrio-ventricular bundle or its limbs, is the real criterion of conducting system fibres, and not peculiarities of histological appearance.

In conclusion, we would like to say that we are fully conscious of the incomplete nature of our present work due to the limitations imposed by the study of blocks and dissections. On this account we have not attempted to give in this paper complete topographical descriptions of the nodes, the atrio-ventricular bundle or its limbs; we have not described the distribution of the limbs of the bundle; and we have not fully surveyed the extent of the sinu-atrial node or the possibility of internodal connections in the atria. We hope to undertake further study of these matters in sections of entire hearts which are now being prepared.

SUMMARY

1. The conducting system of the human and bovine hearts has been studied with the aid of a pyridine silver histological technique evolved by experimental modification so as to secure good impregnation of nerve fibres and at the same time clear differentiation of striated muscle fibres with the minimal amount of shrinkage, even in large blocks.

2. The technique employed emphasises the undoubted muscular nature of both sinu-atrial and atrio-ventricular nodes.

3. The extent of the sinu-atrial node beyond the customarily recognised limits is noted, and its bearing on experimental work in this region of the heart is discussed.

4. The connections of the sinu-atrial nodal fibres with the sinus and atrial musculature and with the musculature of the nodal artery and its branches are described.

5. In the bovine heart, continuity of the sinu-atrial nodal fibres with large "typical" Purkinje fibres, and of these in turn with ordinary atrial muscle fibres, is described, and a parallel drawn with the condition previously observed in the avian heart.

6. A description is given of the structure of the atrio-ventricular node, of the atrial prolongations of the node, and of the continuity of the nodal fibres with those of the atrial myocardium and of the atrio-ventricular bundle.

7. The structure of the fibres of the atrio-ventricular bundle and the proximal parts of its limbs is described.

8. The relative sizes of the muscle fibres of the sinu-atrial node, atrio-ventricular node, atrio-ventricular bundle, atrial myocardium and ventricular myocardium are noted in the human and bovine heart.

9. The general arrangement of nerve cells in relation to the conducting system is noted, and the occurrence of pale and dark staining types (with the silver technique employed) is observed.

10. Two types of nerve ending are noted in relation to the conducting system muscle fibres:

(*a*) A fine perifibrillar network, epilemmal in position, and possibly of afferent function.

(*b*) A simple filiform ending, hypolemmal in position, somewhat similar to the motor nerve ending of skeletal muscle, which may be the motor nerve ending of the conducting system fibres.

11. The presence of nerve fibres with intra-protoplasmic endings has been demonstrated in the tunica media of branches of the coronary arteries.

12. The use of the term Purkinje fibres is discussed.

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EXPLANATION OF PLATES

(All figures are untouched photomicrographs)

PLATE I

Fig. 1. Sinu-atrial node. Ox. ×15. Shows extent of node from epicardium (above) to endocardium (below), with sinus muscle on right and atrial muscle on left.
Fig. 2. Sinu-atrial node. Human. ×46. Shows extent of node from epicardium on right to endocardium on left below, with sinus muscle at lower edge and atrial muscle above and on left.
Figs. 3 and 4. Sinu-atrial node. Ox. ×100. Fig. 3 shows subepicardial nodal fibres and Fig. 4 subendocardial nodal fibres from same section.

PLATE II

Fig. 5. Artery of sinu-atrial node. Ox. ×115. Shows nodal fibres encircling artery.
Fig. 6. Sector of artery of sinu-atrial node. Ox. ×730. Shows striated nodal fibres invading media (on right).
Fig. 7. Sector of artery of sinu-atrial node. Human. ×400. Shows striated nodal fibres approaching media (lumen below on left).
Fig. 8. Right atrium in vicinity of sinu-atrial node. Ox. ×100. Shows tongues of atrial muscle extending amongst plain muscle of endocardium (on right).

PLATE III

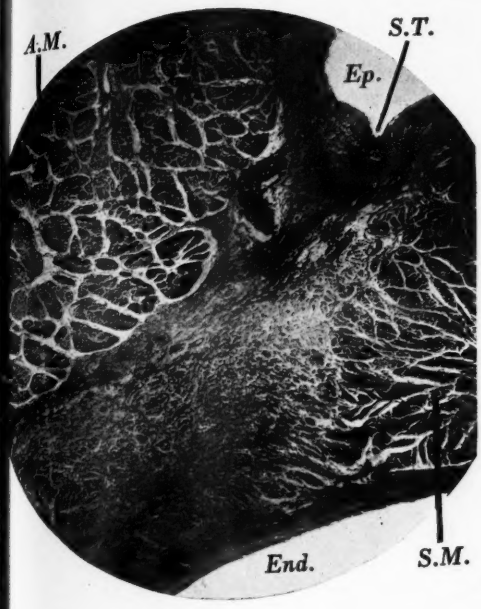
Fig. 9. Sinu-atrial node. Human (14 years). ×400.
Fig. 10. Atrio-ventricular node. Human (14 years). ×400.
Fig. 11. Atrio-ventricular bundle. Human (14 years). ×400.
Fig. 12. Ventricular muscle. Human (14 years). ×400.

PLATE IV

Fig. 13. Atrial muscle. Human (14 years). ×400.
Fig. 14. Edge of sinu-atrial node. Ox. ×460. Shows a nodal fibre lying horizontally in centre of figure establishing continuity by side processes with atrial myocardial fibres above it.
Fig. 15. Right atrium near sinu-atrial node. Ox. ×100. Shows Purkinje fibres in epicardium (below and to right) and extending (above) between bundles of atrial muscle.
Fig. 16. Similar region to fig. 15. Ox. ×260. Shows epicardial Purkinje fibres becoming continuous above with atrial muscle fibres.

PLATE V

Fig. 17. Sinu-atrial node. Ox. ×400.
Fig. 18. Atrio-ventricular node. Ox. ×400.
Fig. 19. Junction of atrio-ventricular node (above) with atrio-ventricular bundle (below). Ox. ×144.



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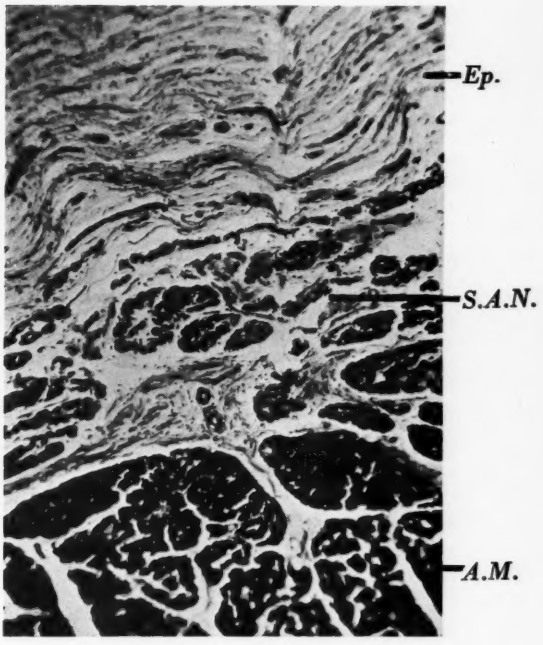

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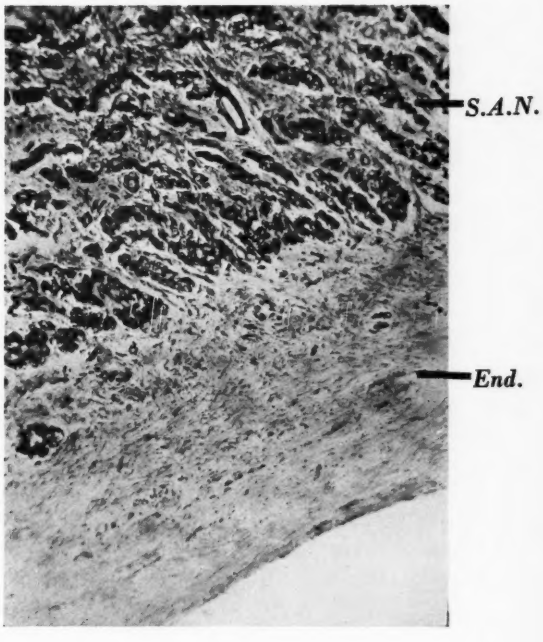

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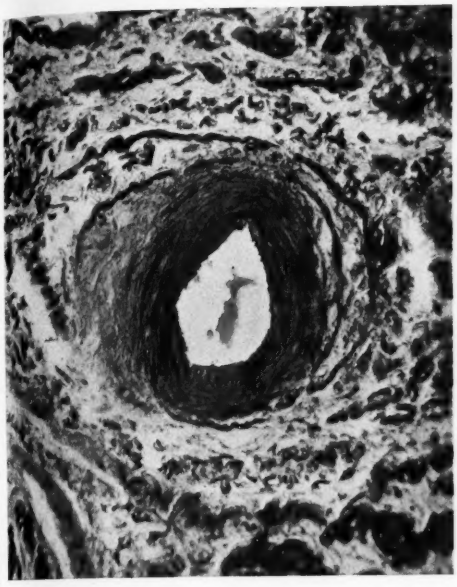

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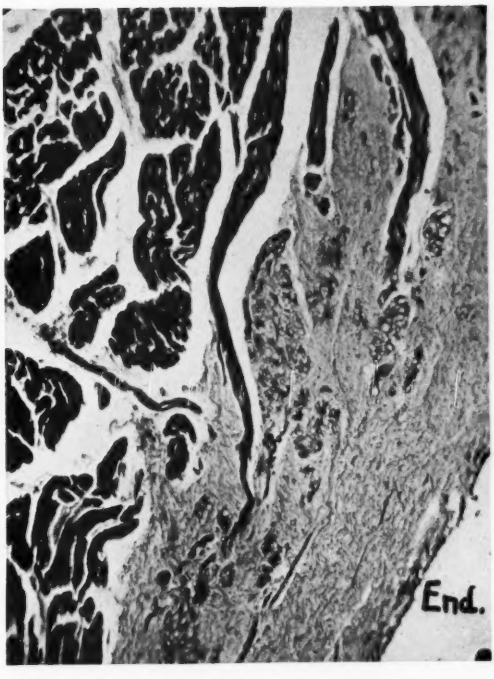

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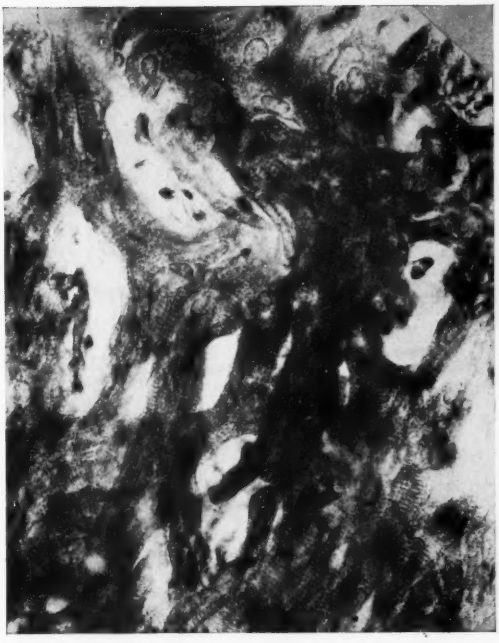

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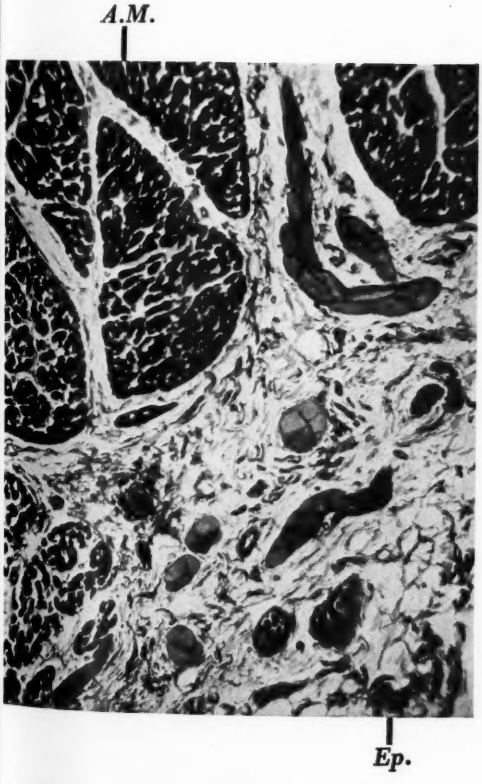

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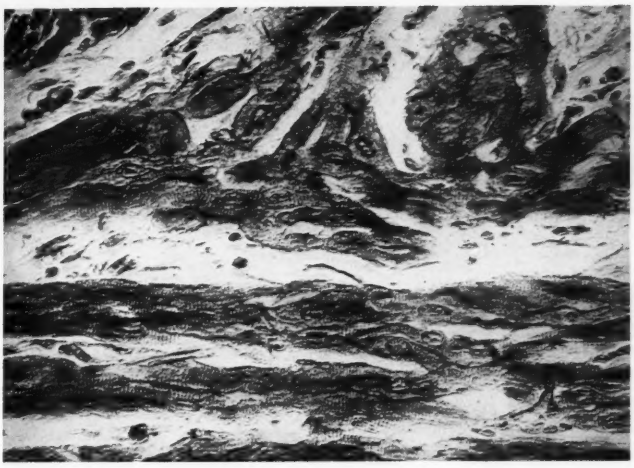

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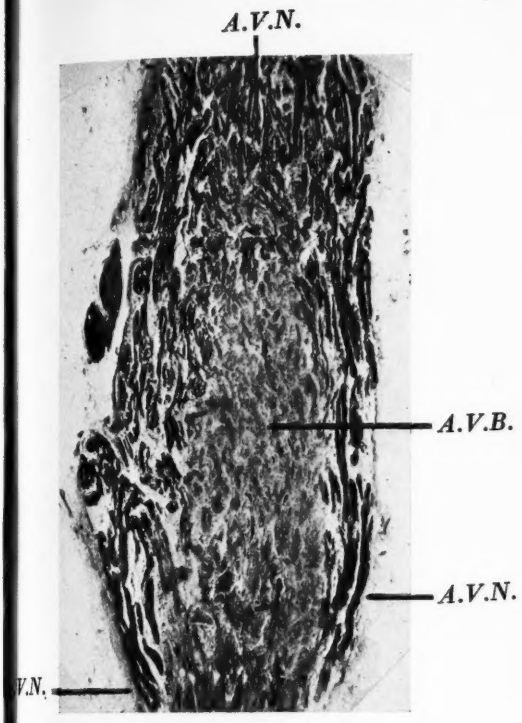

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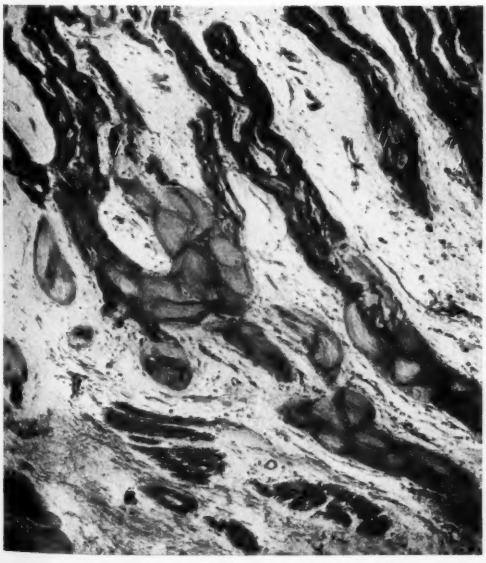

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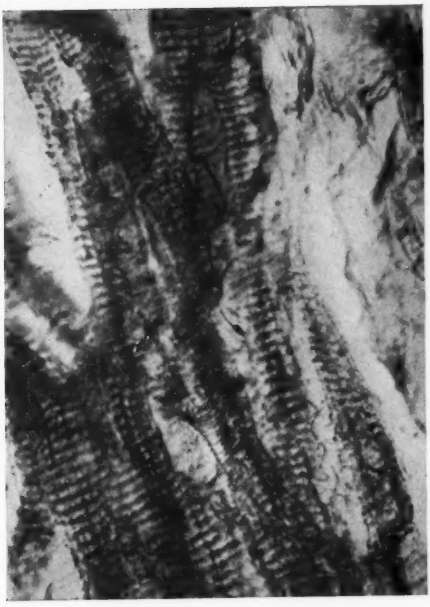

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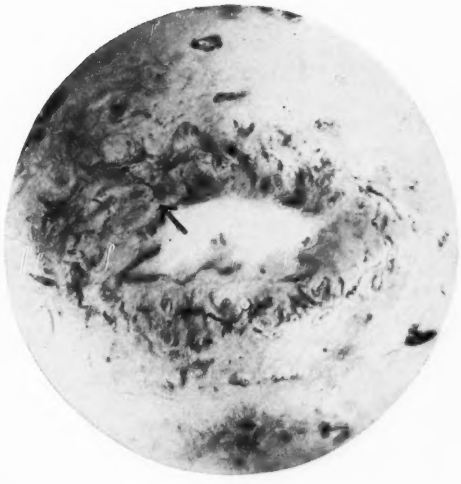

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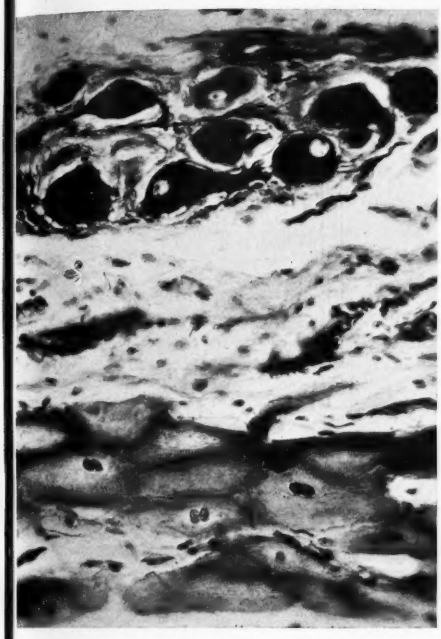

Fig. 28.

Fig. 29.

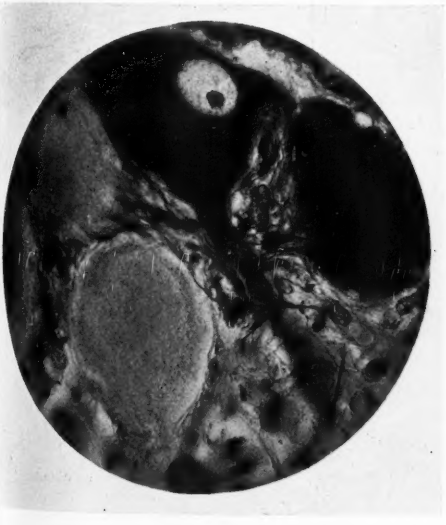

Fig. 30.

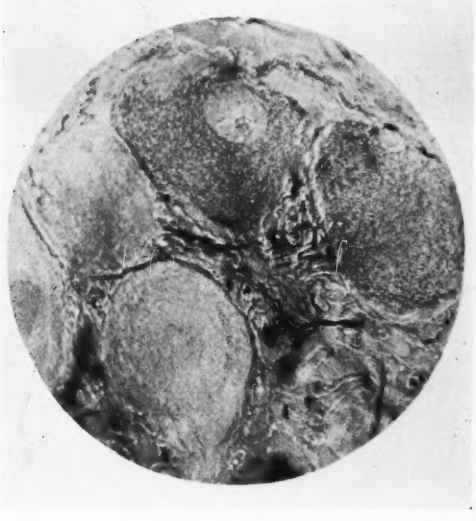

Fig. 31.

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PLATE VI

Fig. 20. Origin of atrio-ventricular bundle (pale fibres) from centre of atrio-ventricular node (dark fibres). Ox (dissected specimen). × 15.

Fig. 21. Atrio-ventricular bundle. Ox. × 40. Shows Purkinje fibres, nerve fibres and nerve cells.

Fig. 22. Junction of atrio-ventricular node and bundle. Ox. × 90.

Fig. 23. Junction of atrio-ventricular nodal fibres with a Purkinje fibre of bundle. Ox. × 500.

PLATE VII

Fig. 24. Atrio-ventricular bundle. Ox. × 900. Shows nerve fibre ending amidst group of nuclei in relation to Purkinje fibre (see text).

Fig. 25. Atrio-ventricular bundle. Human. × 1100. Shows fine nerve fibre in upper half of figure running downwards with sinuous course between bundle fibres and ending in terminal enlargement on left side of a striated bundle fibre. Striations of muscle fibre can be seen, in a slightly different focal plane to that photographed, to approach still more closely to the nerve ending. (See text.)

Fig. 26. Purkinje fibre from left limb of atrio-ventricular bundle. Ox. × 400. Shows peripherally placed nuclei.

Fig. 27. Branch of coronary artery. Ox. × 500. Infra-red plate. Shows nerves in media with paranuclear terminal loop in upper left quadrant. (↑.)

PLATE VIII

Fig. 28. Left limb of atrio-ventricular bundle. Ox. × 260.

Fig. 29. Right limb of atrio-ventricular bundle. Ox. × 260.

Figs. 30 and 31. Nerve cells in wall of right atrium. Ox. × 700. Fig. 30 panchromatic plate and fig. 31 infra-red plate. Shows dark and pale types of nerve cells.

ABBREVIATIONS USED IN FIGURES

A.M.	Atrial myocardium.	*Ep.*	Epicardium.
A.V.B.	Atrio-ventricular bundle.	*S.A.N.*	Sinu-atrial node.
A.V.N.	Atrio-ventricular node.	*S.M.*	Sinus myocardium.
End.	Endocardium.	*S.T.*	Sulcus terminalis.

THE GROWTH OF THE PELVIS IN THE MADDER-FED PIG

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By general observations of bone deposit and absorption it will be shown that the bones forming the pelvis grow in the same way as those of the extremities, i.e. by additions at each end of their long axes—corresponding to diaphysial growth of the long bones—and these additions are modified by absorption areas, as in the long bones, before they become incorporated with the body of the bone at a later stage. The body of each bone shows a layer of new bone on its surface, increasing its thickness in proportion to the increasing size of the extremities—a process which takes place in any long bone—but owing to the peculiar position of these bones in relation to the pelvic cavity, these surface additions are necessarily made only on their external surfaces relating to the pelvic cavity.

By measurements and calculations, throughout a total growth period of 199 days, the increments at the extremities of each pelvic bone will be shown to account accurately for the actual increase in length of each pelvic bone.

The pelvic bones will be shown to be disposed round the pelvic brim so that their growing extremities increase either the side-to-side or antero-posterior diameters, but not both. Consequently, it will be anticipated that, by noting which extremity involves a particular diameter, it might be possible to account for the increase in pelvic diameters. Actually the increase in side-to-side diameter can be accounted for in this way, but not the antero-posterior diameter, which actually increases much in excess of the expected. This unexpected excess of the actual antero-posterior diameter over the expected will be shown to be due to an interesting movement in a cranial direction of the sacro-iliac articulation.

The great sciatic notch will also be shown to move cranially, keeping pace with the sacro-iliac articulation.

The obturator foramen will be shown to keep almost equidistant from the symphysis pubis, although new bone is constantly being laid down at the symphysial end of the pubis. This power of movement has previously been pointed out in respect to the nutrient foramina of the long bones (1).

The literature dealing with the "Growth of the Pelvis" is scanty. Kölliker (2) notes the position of the more important absorption areas of the innominate bone, including one around the lower part of the obturator foramen, but he

makes no attempt to relate them to the growth of the pelvis as a whole. Quain (3), quoting Merkel (4), states that enlargement of the cavity is due to increase in width of the sacrum in its lateral costal parts and especially to growth of the part of the ilium between the sacrum and acetabulum.

MATERIAL AND METHODS

Observations and measurements are made from the pelves of a dozen madder-fed pigs belonging to the same series as used for my recent published investigation on diaphysial growth (5), and placed at my disposal by Prof. Brash. The age of the pigs varied from 80 to 587 days. These pigs had been treated by the "indirect madder method", whereby the madder is withheld for a period before killing, and consequently the new bone of this non-madder period shows up white against a background of maddered bone.

Particulars of age, madder period, and non-madder period are noted in Table I.

Table I. *Duration in days with and without madder feeding*

Pig No.	Age at death days	Madder period days	Non-madder period days
14	80	72	8
15	91	77	14
16	108	84	24
17	126	105	21
12	140	61	28
1	169	68	29
2	197	97	28
3	225	125	28
4	279	153	54
6	362	207	84
9	475	271	126
8	587	394	116

The maximum length of each pelvic bone is taken on the osteometric board. The lengths of the ilia are the maximum distances between the antero-superior spine and the acetabulum, while the breadth is the distance between the antero- and postero-superior spines. The lengths of the ischia and pubes are the maximum distances between the acetabulum and the tuberosity or symphysis respectively.

In order to obtain reasonably accurate measurements of the amount of new bone added to the ends of these bones, sections are cut in the same plane used for measurement of maximum length and approximately sagittal for ilia and ischia, and approximately coronal for pubes.

Sections of the sacra are made through the first piece in a dorso-ventral plane as explained in the text.

The pelvis is formed by the two innominate bones and the sacrum (fig. 1).

The *innominate bone* consists of the ilium, ischium and pubis; these three parts meet at the acetabulum.

The *ilium* forms the anterior expanded portion of the innominate bone and presents for examination a body with an expanded extremity at each end.

The body is the constricted portion of the ilium and generally speaking in the majority of specimens shows a deposit of new white bone which surrounds it in the form of a band. This band of new bone is more extensive on the lateral than the medial surface (fig. 2).

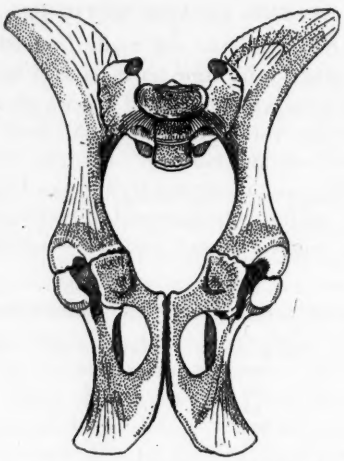

Fig. 1. Pelvis. Pig No. 4. Scale $\times \frac{1}{4}$. Age 279 days. Madder period 153 days, non-madder period 54 days. Areas of bone unstained by madder are represented white and indicate new bone laid down during the second non-madder period 54 days. Bone stained by madder is stippled.

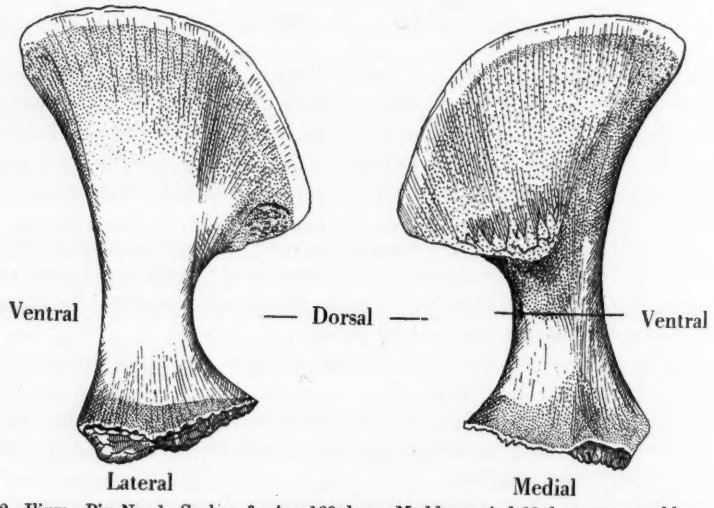

Fig. 2. Ilium. Pig No. 1. Scale $\times \frac{3}{4}$. Age 169 days. Madder period 68 days, non-madder period 29 days. New bone represented white and madder-stained bone stippled as in fig. 1.

The cranial margin of the new bone on the lateral surface is convex towards the crest of the bone, and in most of the specimens it reaches farther in a cranial direction towards the anterior than the posterior border. At the posterior border it generally lies level with the deepest part of the great sciatic notch. On the medial surface the cranial margin of new bone is generally concave towards the articular surface for the sacrum and extends nearer the crest of the bone in relation to the anterior than the posterior border of the bone. In some specimens this new bone on the medial surface does not stretch from the anterior to the posterior border, but is confined to the anterior half of this surface.

The caudal margin of the area of new bone on the lateral surface is, in most specimens, almost straight; but in a few specimens it slopes caudally towards the posterior border, when the new bone of the body becomes continuous with the new bone on the caudal or acetabular end of the bone. On the medial surface this caudal margin of new bone varies considerably. In some bones it is convex cranially, while in others it is almost absent, since the new bone is confined to the anterior half of the surface and the remainder is occupied by an area of old red bone.

On each extremity there is a layer of new bone which is thicker, in a cranio-caudal direction, at the crest end than at the acetabular end of the bone. On the medial and lateral surfaces of both these layers of new bone there are absorption areas. The absorption areas of the new bone at the crest end are most extensive at the anterior and posterior borders of the medial and lateral surfaces, and also just below the articular surface for the sacrum on the medial aspect. At the acetabular end the absorption areas of new bone are most extensive towards the front of the lateral and medial surfaces. In the majority of specimens absorption is absent in relation to the posterior border of the acetabular end of the bone.

On examining a longitudinal section cut in a side-to-side plane, new bone is seen on both surfaces in the form of a layer, which tapers off towards each end (fig. 3). The longitudinal section shows, on the medial side and towards the anterior end, another layer of new bone, which covers the auricular surface of the ilium for articulation with the sacrum. This layer of new bone is a continuation of the new bone on the anterior extremity of the bone.

A cross-section through the middle of the body shows this layer of new bone surrounding the outside of the bone. It is much thicker on the external aspect (fig. 4).

The nutrient foramen is situated on the inner surface close to the dorsal border. It lies close to the anterior margin of the layer of new bone round the body of the bone, and enters the bone in an antero-posterior direction.

The *anterior extremity* forms the crest of the ilium and is covered by a layer of new bone. The maximum breadth of this new bone has been measured from antero- to postero-superior spines and the measurements from the youngest bone and an older one are contrasted No. 14 (80 days) 5·9 cm., No. 4

(279 days) 8·1 cm., the older bone showing an increase of 2·2 cm., and the difference in age of the two bones being 199 days.

This constant increase in breadth by the growth of new bone, if unchecked, would ultimately give a very large expansion to this end of the bone; but this is avoided by an area of absorption distal to this layer of new bone, in the form of a band which is widest in relation to the anterior and posterior borders. The absorption area in relation to the posterior border involves the anterior border

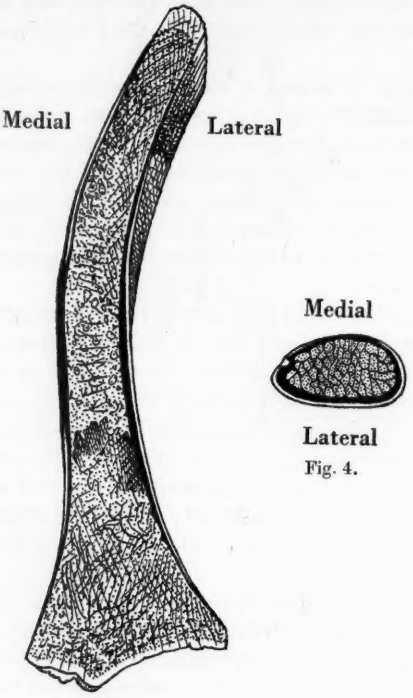

Fig. 4.

Fig. 3.

Fig. 3. Longitudinal section of ilium (Pig No. 1), as detailed in fig. 2, to show new bone at the crest and acetabular ends together with a thin layer of new bone on the lateral surface.

Fig. 4. Cross-section through body of ilium (Pig No. 1) to show the thin layer of new bone on the lateral surface.

of the great sciatic notch to which reference will be made later. By superimposing the layer of new bone of the anterior extremity upon a cross-section through the body of the ilium some idea may be obtained of the amount of absorption necessary to bring the successive layers of new bone into proportion with the body of the bone (fig. 5).

The acetabular extremity is triangular in shape, and forms the anterior margin of the acetabulum. It is occupied by a layer of new bone. The greatest

ventro-dorsal and side-to-side diameters of this layer of new bone have been measured from the youngest and an older bone:

No. 14 (80 days): ventro-dorsal 36·0 mm., side-to-side 28·2 mm.
No. 4 (279 days): ,, 51·0 mm., ,, 34·7 mm.

The older bone, No. 4, shows an increase in its ventro-dorsal diameter of 15·0 mm. and in its side-to-side diameter 6·5 mm., the difference in age of the two bones being 199 days.

This layer of new bone forms three distinct areas, one situated ventro-laterally, forming part of the acetabulum and covered in the recent state by cartilage; another situated dorsally, uncovered by cartilage in the recent state and showing the sharp ends of bony spicules which form with the ischium a

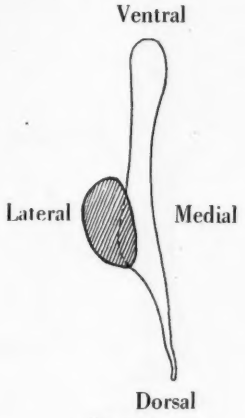

Fig. 5.

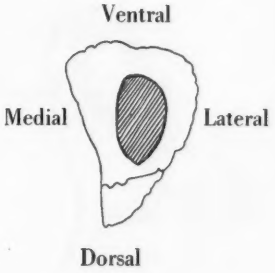

Fig. 6.

Fig. 5. Outlines of crest and body, as in fig. 4, of ilium superimposed to illustrate the amount of absorption necessary to bring the crest into proportion with the body.

Fig. 6. Outlines of acetabular end of body of ilium again superimposed, as in fig. 5, to show the amount of absorption necessary to bring the acetabular end into proportion with the body of the bone.

synostosis; and lastly an intermediate area separating the above two surfaces, covered with cartilage which comes into relation to the ischium and pubis.

This layer of new bone is separated from that on the body of the bone by an absorption area which is absent dorsally, in which position the posterior margin of the great sciatic notch is situated. By superimposing this layer of new bone upon a section through the body of the bone, an idea may be obtained of the amount of absorption which is necessary to bring the successive layers of new bone into proportion with the body of the bone (fig. 6).

The *ischium* consists of a body and an expanded extremity at each end. One extremity is anterior and takes part in the acetabulum, the other extremity is posterior, supports an epiphysis for the tuberosity, and has a ventral projection—the ramus.

The body is compressed from side to side and has prominent ventral and dorsal margins separating medial and lateral surfaces. There is a deposit of new white bone on the body which extends on the lateral surface, uninterruptedly from the ventral to the dorsal margins; on the medial surface the new bone is, in the majority of specimens, confined to the neighbourhood of the ventral and dorsal margins, the intervening part being occupied by an area of old red bone. Towards the ventral margin the new bone forms part of the boundary of the obturator notch to which reference will be made later.

The margin of the new bone extends further anteriorly near the dorsal border than it does along the ventral border and is separated from the acetabular area by an absorption area, except close to the dorsal border, where in most specimens it becomes continuous with a layer of new bone on the acetabular extremity of the bone.

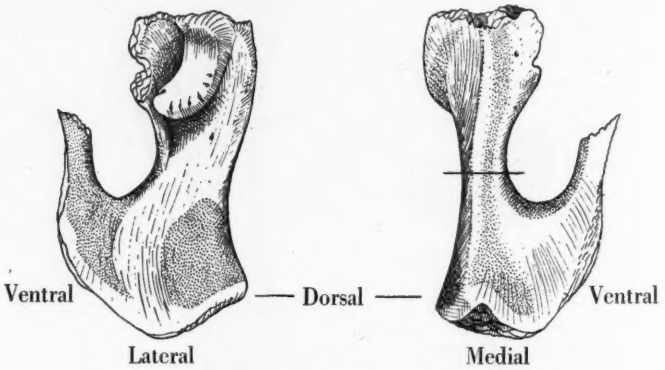

Fig. 7. Ischium. Pig No. 1. Scale $\times \frac{2}{3}$. Details as in fig. 2.

The posterior margin of new bone on the lateral surface comes into relation to some old red bone close to the ischial tuberosity. In most of the specimens it is concave towards the posterior end of the bone, and stretches farther towards the ischial tuberosity near the ventral than the dorsal margins. In some specimens it becomes continuous along the ventral margin with the new bone on the posterior extremity. On the internal aspect the posterior margin is absent, as the new bone does not extend completely over this surface.

On examining a section cut through the long axis of the bone in a side-to-side plane, the new bone is seen in the form of a layer which tapers towards each end and which is most extensive on the external surface (fig. 8). A transverse section shows this new bone on the external surface (fig. 9).

Measurements of the greatest side-to-side diameter have been made from the youngest and an older bone for contrast: No. 14 (80 days) 7·5 mm., No. 4 (279 days) 9·0 mm. The older bone shows an increase of 1·5 mm. and is 199 days older than No. 14.

This increase in width is chiefly due to increments of new bone on the external surface.

The *anterior extremity* enters into the formation of the acetabulum, is triangular in shape and is covered by a layer of new bone. Its greatest ventro-dorsal and side-to-side diameters have been measured from the youngest and from an older bone:

No. 14 (80 days): ventro-dorsal 23·1 mm., side-to-side 23·1 mm.
No. 4 (279 days): ,, 32·8 mm., ,, 28·1 mm.

The older bone shows an increase of 9·7 mm. in its ventro-dorsal, and 5·0 mm. in its side-to-side diameters.

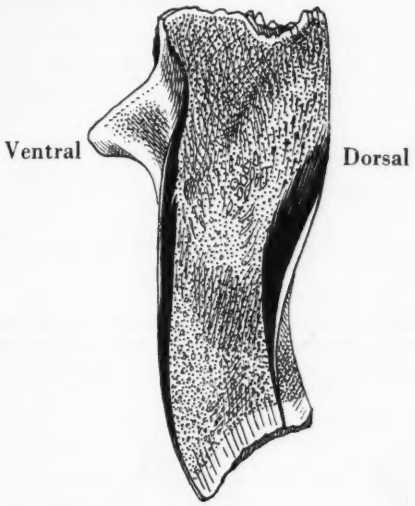

Fig. 8.

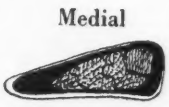

Fig. 9.

Fig. 8. Longitudinal section of ischium, as in fig. 7, to show new bone at acetabular and tuberous ends.

Fig. 9. Cross-section through body of ischium, as in fig. 7, to show new bone mainly on lateral surface.

The greater part of the extremity supports a cartilage-covered surface for the ilium. Dorsally there is a small non-cartilaginous area also for the ilium. Ventro-laterally there is a cartilage-covered area forming part of the acetabulum. Ventro-medially there is a cartilage-covered area which comes into contact with the pubis.

Separating this layer of new bone from the body is an absorption area which is most extensive round the lateral aspect of the acetabulum. By superimposing this new bone of the anterior extremity upon a section through the body of the bone, some idea may be obtained of the amount of absorption necessary to bring the successive plates of new bone into proportion with the body (fig. 10).

The *posterior extremity* forms the tuberosity. It is covered by a layer of new bone which is triangular in shape, with an apex placed medially and prolonged towards the ramus. The greatest ventro-dorsal and side-to-side diameters have been measured from the youngest and from an older bone for contrast:

No. 14 (80 days): ventro-dorsal 16·5 mm., side-to-side 18·0 mm.
No. 4 (279 days): ,, 21·5 mm., ,, 25·3 mm.

The older bone No. 4 shows an increase of 5·0 mm. in its ventro-dorsal diameter and 7·3 mm. in its side-to-side diameter.

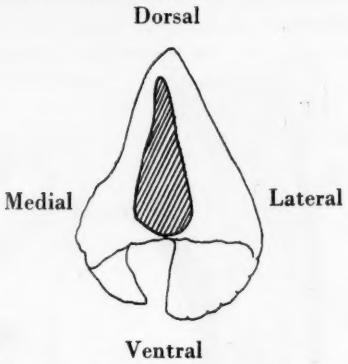

Fig. 10. Outlines of acetabular end and body, as in fig. 9, superimposed to illustrate the amount of absorption necessary to bring the acetabular end into proportion with the body.

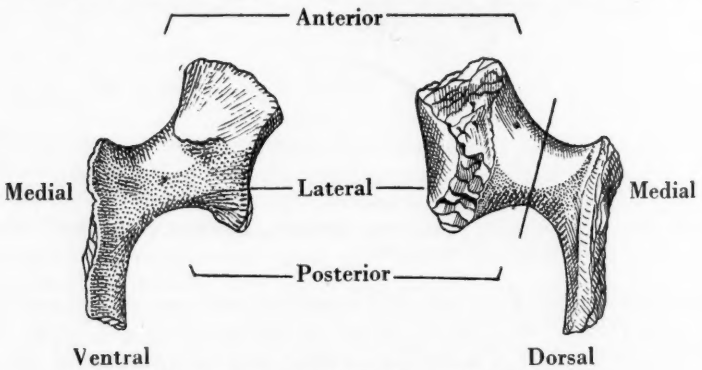

Fig. 11. Pubis. Pig. No. 1. Scale nat. size. Details as in fig. 2.

The plate of new bone is separated from the body by an absorption area which is most extensive on the medial and lateral surfaces; but is absent on the ventral border where the successive plates of new bone project and form the ramus.

The *pubis* is a cylindrical-shaped bone presenting for examination a body and two enlarged extremities (fig. 11).

The cylindrical-shaped body is somewhat compressed, so that it has lateral and medial surfaces, separated by anterior and posterior margins. Generally the new white bone is situated towards the anterior margin of the lateral and medial surfaces, while towards the posterior margin there is an area of old red bone on both surfaces to which reference will be made under "Obturator foramen". On the lateral surface the new bone is continuous laterally with the new bone at the acetabular end, and towards this end the area of new bone on the body is most extensive. Towards the symphysial end the area of new bone on the lateral surface is narrow and separated from the new bone of the symphysial end by an area of old red bone. On the medial surface the new white bone stretches from the layer of new bone on the acetabular end to within a short distance of the new bone on the symphysial extremity. It is more extensive towards the middle of the body and here the new bone has a margin, convex posteriorly, where it meets the old red bone towards the posterior border.

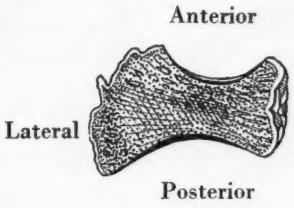

Fig. 12.

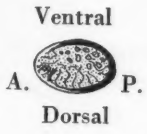

Fig. 13.

Fig. 12. Section through the long axis of pubis, as in fig. 11, to show layers of new bone at lateral and medial ends.

Fig. 13. Cross-section through body of pubis, as in fig. 11, to show layer of new bone mainly towards anterior border.

A section through the long axis of the bone cut in an antero-posterior plane shows this new bone in the form of a layer which tapers towards each end (fig. 12). The posterior surface is mainly occupied by an absorption area. A transverse section through the middle of the bone shows this deposit of new bone on the external and internal surfaces towards the anterior border (fig. 13).

The acetabular end is oval and covered by a layer of new bone, the maximum diameters of which have been measured in an antero-posterior and a ventro-dorsal plane from the youngest and an older bone:

No. 14 (80 days): antero-posterior 21·0 mm., ventro-dorsal 17·5 mm.
No. 4 (279 days): ,, 29·5 mm., ,, 24·4 mm.

The older bone shows an increase of 8·5 mm. in its antero-posterior and 6·9 mm. in its ventro-dorsal diameters.

The new bone at the acetabular end is divided into four areas. A central non-articular area, forming part of the floor of the acetabulum; dorsally, there is a cartilage-covered surface for the ischium; anteriorly, there is a similar

cartilage-covered surface for the ilium; and ventrally, there is a smooth surface forming the pubic part of the articular surface of the acetabulum.

Medial to this layer of new bone there is an area of absorption which is most extensive on the dorsal aspect.

The symphysial end is covered by a layer of new bone which is wedge-shaped, the base being anterior. The maximum diameters of this new bone have been measured in an antero-posterior and a ventro-dorsal plane from the youngest and from an older bone:

No. 14 (80 days): antero-posterior 25·3 mm., ventro-dorsal 14·5 mm.
No. 4 (279 days): ,, 29·0 mm., ,, 18·0 mm.

The older bone shows an increase of 3·8 mm. in its antero-posterior diameter and 3·5 mm. in its ventro-dorsal diameter.

The whole of the symphysial layer of new bone is covered by a layer of cartilage in the recent state.

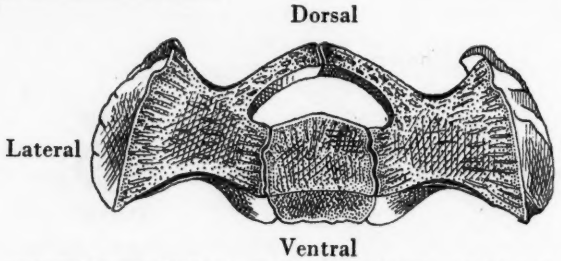

Fig. 14. Section of sacrum (Pig No. 1) cut in a frontal plane, as in fig. 2, to show layers of new bone on lateral and medial surfaces of alae and lateral surfaces of centrum.

Lateral to this plate of new bone is an absorption area which is most extensive towards the posterior border, which comes into relation with the medial margin of the obturator foramen, to which reference will be made later.

The sacrum. The first and second pieces of the sacrum articulate laterally with the ilium on each side (fig. 1). Each piece consists of two lateral processes and a centrum. Each lateral process forms the lateral third of the body, the wing and half of the neural arch behind, while the centrum completes the middle third of the body.

The lateral processes show additions of new bone very similar to those seen on the long bones. There is a layer of new bone at the lateral and medial ends corresponding to the layer of new bone at the diaphysial ends of the long bones; each of these additions is separated by an area of absorption from a layer of new bone situated round the middle of each process, this layer corresponds to that round the shaft of a long bone.

A section through the middle of the first piece of the sacrum in a ventro-dorsal plane shows these additions of new bone on the lateral and medial ends, and also the new bone in the form of a surface layer in relation to the middle of each lateral process (fig. 14). The layer of new bone at the lateral end of this process is concerned with the increment at the sacro-iliac junction.

The centrum shows a layer of new bone on its cranial and caudal surfaces, with an area of absorption separating these two layers on its ventral surface. There is a thin layer of new bone on its lateral surface and this, together with the new bone already described on the medial surface of the lateral process, forms the increment to the size of the pelvic cavity at the junction of the lateral and central parts of the sacrum.

The growth of the bones forming the pelvis has been considered with a view to considering the growth of the pelvis as a whole and especially the growth of the cavity of the pelvis. Measurements of the antero-posterior diameter (from the back of the symphysis pubis to the anterior border of the ventral surface of the sacrum, i.e. the promontory), and of the maximum transverse diameter at right angles to the antero-posterior diameter have been made from the youngest and oldest pelves:

No. 14 (80 days): antero-posterior 51·3 mm., transverse 50·2 mm.
No. 8 (587 days): ,, 78·3 mm., ,, 69·3 mm.

The older pelvis increases the size of its cavity by 27 mm. antero-posteriorly and 19·1 mm. transversely.

These measurements expressed in terms of the pelvic brim index

$$\frac{\text{Antero-posterior diameter} \times 100}{\text{Transverse diameter}}$$

give the following results:

$$\text{No. 14, } \frac{51{\cdot}3 \times 100}{50{\cdot}2} = 102{\cdot}19; \quad \text{No. 8, } \frac{78{\cdot}3 \times 100}{69{\cdot}3} = 112{\cdot}97.$$

These indices show that the difference in proportion between the two diameters alters so that in the older pelvis the antero-posterior diameter becomes relatively longer than the transverse.

It has already been observed that the three bones forming the innominate, increase the length of their long axes by the addition of successive layers of new bone added to each end of the long diameter. These bones are grouped round the cavity of the pelvis so that at least one end of each of their long axes is included in the wall of the pelvic cavity. In addition to the innominate bone on each side, the centrum and lateral processes of the sacrum enter into the wall of the pelvic cavity behind, and consequently the layers of new bone observed on the adjacent ends of the centrum and lateral processes together with that on the lateral ends of these processes contribute to the growth of the pelvic cavity.

Passing round the wall of the pelvic cavity from the symphysis pubis to the middle of the sacrum, increments of new bone are observed in the following positions:

(1) The pubic symphysis.
(2) The junction between pubis, ilium and ischium at the acetabulum.
(3) Sacro-iliac junction.
(4) The junction of the lateral part and centrum of the first and second

pieces of the sacrum, and also the junction behind, in the middle line, of the neural arches of these pieces of the sacrum.

The *obturator foramen* is situated towards the front of the pelvis, and is oval in shape with its long diameter in a cranio-caudal plane (fig. 1). It is bounded medially and cranially by the pubis and laterally and caudally by the ischium. Measurements of the maximum cranio-caudal and side-to-side diameters have been made from the youngest and oldest pelves for contrast:

No. 14 (80 days): cranio-caudal 21·0 mm., side-to-side 15·0 mm.
No. 8 (587 days): „ 44·5 mm., „ 28·0 mm.

The older pelvis shows an increase in the diameters of its obturator foramen of 23·5 mm. for the cranio-caudal and 13·0 mm. for the side-to-side diameters.

An examination of the margins of this foramen shows that the pubo-ischial junctions are situated in relation to the medial and lateral walls, so that the layers of new bone added to these bones at their junctions increase the cranio-caudal diameter of the foramen.

There is no bony junction in either the cranial or the caudal walls of the foramen: but on the medial wall there is an absorption area extending over the whole length of this wall and controlling the thickness of bone between the symphysis pubis and the medial side of the obturator foramen. A layer of new bone has been described on the symphysial end of the pubis. By measuring the maximum thickness of bone between the symphysis pubis and the medial border of the obturator foramen in bones of various ages, it can be shown that the actual increase in thickness due to the successive layers of new bone at the symphysial end of the pubis is very slight owing to the absorption of bone on the medial wall of the foramen:

No. 14 (80 days): thickness of bone referred to above 5·7 mm.
No. 8 (587 days): „ „ 6·3 mm.

The older pelvis shows the small increase of 0·6 mm. (It will be shown later that the increment per week at the symphysial end of the pubis varies from 0·75 mm. in the youngest (No. 14) to 0·09 mm. in No. 4 (279 days).)

The lateral wall of the foramen is formed by the body of the ischium which is immediately posterior to the acetabulum. The ventral surface of the body of the ischium forms the wall in question and is covered by a thin layer of new bone.

The chief factor that is responsible for the increase in side-to-side diameter of the obturator foramen is the absorption area on its medial wall, and further, this absorption area also keeps the medial margin almost equidistant from the middle line of the body. (There is only 0·6 mm. difference in the two pelves whose ages differ by 507 days.)

The *great sciatic notch* is bounded by the dorsal border of the ilium (fig. 2). It has been observed that the anterior or cranial margin of the notch shows an area of absorption continuous with that which modifies the layers of new bone added to the anterior end of the ilium. The posterior margin is occupied by a layer of new bone continuous with that added round the body of the ilium.

The maximum distance between the two edges of this notch have been measured from a point at which the ilium articulates with the ischium below to the postero-inferior spine above, and the measurements from the youngest and oldest bones are contrasted: No. 14 (80 days) 30 mm., No. 8 (587 days) 67·5 mm. The older bone shows an increase of 37·5 mm. This increase in size is mainly due to the absorption of bone from its anterior wall in which direction the notch extends.

MEASUREMENTS OF THE PARTS OF THE INNOMINATE BONES

The lengths of the ilia are the maximum distances between the antero-superior spine and the acetabulum, while the breadth is the distance between the antero- and postero-superior spines.

The lengths of the ischia and pubes are the maximum distances between the acetabulum and the tuberosity or symphysis respectively.

Table II. *Measurements in cm. of parts of innominate bones*

Pig. no.	14	15	16	17	12	1	2	3	4
Age in days ...	80	91	108	126	140	169	197	225	279
Ilia: Length	8·4	8·5	8·7	9·8	10·1	10·1	11·0	11·5	12·3
Breadth	5·9	5·6	5·4	6·6	6·7	7·9	7·2	7·8	8·1
Ischia: Length	6·5	6·5	6·7	7·5	7·5	7·3	8·0	8·4	9·7
Pubes: Length	2·3	2·2	2·4	2·5	2·8	2·9	3·0	3·1	3·2

The ilium is the longest of the three parts of the innominate bone. The ischium is intermediate and the pubis is the smallest.

Sections of the three parts of the innominate were made through the long axes and in the same planes as the measurements of length were made (figs. 3, 8 and 12). The maximum thickness of new bone at each end of the long axes could thus be measured.

Table III. *Measurements in mm. of the increments made to the two ends from which the lengths were measured*

Pig. no.	14	15	16	17	12	1	2	3	4
Age of new bone in days	8	14	24	21	28	29	28	28	54
Ilia: Crest end	3·7	4·2	5·0	5·4	5·8	4·0	3·5	3·0	5·0
Acetabular end	1·1	1·5	1·3	1·6	1·8	1·4	1·0	0·8	1·1
Ischia: Acetabular end	0·9	1·6	1·8	0·9	1·5	1·2	0·9	0·6	0·75
Tuberous end	2·5	3·0	3·0	3·6	3·9	3·7	3·6	3·0	3·0
Pubes: Acetabular end	0·25	0·45	0·40	0·25	0·30	0·30	0·25	0·25	0·35
Symphysial end	0·75	1·0	1·85	1·0	1·1	1·0	0·65	0·5	0·75

It is observed that the increments to the lengths of the parts of the innominate bone consist, as in the case of the diaphysial increments of the long bones (5), of a greater increment at one end and a lesser increment at the other. All the parts of the innominate bone have their lesser increments at their acetabular ends and their greater increments at their ends remote from the acetabulum. The lesser increments at the acetabular ends of the three parts are not of similar amount, that of the ilium being the largest, while that of the pubis is the smallest.

These amounts of growth are for periods increasing in length to compensate for the diminishing rate of growth with the increasing age of the animal. For convenience of comparison these amounts of growth over varying periods have been calculated over a uniform period of one week.

Table IV. *Measurements in mm. of rates of growth per week calculated from* Table III

Pig no.	14	15	16	17	12	1	2	3	4
Ilia: Crest end	3·7	2·1	1·42	1·8	1·4	1·0	0·9	0·75	0·63
Acetabular end	1·1	0·75	0·37	0·52	0·45	0·35	0·25	0·2	0·14
Ischia: Acetabular end	0·9	0·7	0·51	0·33	0·37	0·3	0·22	0·15	0·09
Tuberous end	2·5	1·5	0·9	1·2	0·97	0·93	0·9	0·75	0·37
Pubes: Acetabular end	0·25	0·22	0·1	0·08	0·07	0·07	0·06	0·06	0·04
Symphysial end	0·75	0·50	0·24	0·33	0·27	0·25	0·20	0·12	0·09

From the table to show the rates of growth calculated to one week, it is seen that, as in the case of the diaphyses of the long bones (5) there is a gradual diminution in the rate of growth as one passes from the younger to the older bones. In the case of the diaphysial increments of the long bones, however, it was shown that the greater and lesser increments were generally similar in amount for bones of the same age; this is not the case with the parts of the innominate bones.

The ends of the parts of the innominate bones with the lesser increments are united together at the acetabulum from No. 6 (362 days) onwards.

MEASUREMENTS OF SACRA (FIRST PIECE)

The width of the ala is the maximum distance between the medial and lateral surfaces, and the width of the centrum is half the maximum distance between its lateral surfaces and the sum approximately represents the distance from the middle line to the lateral surface (fig. 14).

Table V. *Measurements in mm. of parts of sacra*

Pig no.	14	15	16	17	12	1	2	3	4	6	9	8
Age in days ...	80	91	108	126	140	169	197	225	279	362	475	587
Width of ala	17·5	17·0	15·0	19·0	16·5	20·0	21·5	24·5	23·0	24·0	21·0	23·0
Width of centrum	8·0	8·0	7·5	9·5	8·5	8·5	9·5	10·0	9·25	10·0	10·0	9·5

Sections of the first piece of the sacrum were cut in a horizontal plane and in the same plane as the measurements of width were made (fig. 14). The maximum thickness of new bone was measured at the medial and lateral ends of the ala and at the lateral end of the centrum.

Owing to the small amount of increment between medial end of ala and lateral end of centrum, the two increments were measured together and divided equally.

Bony union takes place between ala and centrum in No. 6 (362 days).

Table VI. *Measurements in mm. of the increments to the ala and centrum*

Pig. no.	14	15	16	17	12	1	2	3	4	6	9	8
Age of new bone in days	8	14	24	21	28	29	28	28	54	84	126	116
Ala: Lateral end	0·6	0·5	0·5	0·5	0·5	0·5	0·45	0·4	0·6	0·55	0·5	—
Medial end	0·4	0·25	0·35	0·35	0·35	0·25	0·20	0·25	0·2	Fused	—	—
Centrum	0·4	0·25	0·35	0·35	0·35	0·25	0·20	0·25	0·2	Fused	—	—

It is seen that the increments at the two ends of the ala are unequal, the increment on the lateral end which takes part in the sacro-iliac joint being greater than that on the medial end which articulates with the centrum.

For comparison these amounts of growth over varying growth periods have been calculated to a uniform period of one week.

Table VII. *Measurements in mm. of rates of growth per week calculated from* Table VI

Pig no. ...	14	15	16	17	12	1	2	3	4	6
Ala: Lateral end	0·6	0·25	0·15	0·15	0·13	0·13	0·12	0·10	0·08	0·05
Medial end	0·4	0·13	0·10	0·10	0·09	0·06	0·05	0·06	0·03	—
Centrum	0·4	0·13	0·10	0·10	0·09	0·06	0·05	0·06	0·03	—

From this table, showing the rates of growth calculated to a uniform period of one week, there is seen to be a gradual diminution in the rate of growth as one passes from the younger to the older bones.

In my previous investigations into the growth of the diaphyses and epiphyses, a graphic method of contrasting the expected increments—calculated from the growth per week—with the actual increase at twelve given intervals throughout a growth period from 80 to 587 days, was used. A severer and simpler method of contrast is to compare the measurements of the total expected increment with the actual increase. For this purpose it is not practical to go beyond No. 4 (279 days) because after this, fusion of the bones makes measurements difficult.

In Table VIII the difference in age of each successive bone is noted and the expected increment calculated for this period from the growth per week, at that particular age period.

In the case of the sacrum, the width is represented from the middle line, and represents the sum of the widths of the ala and half of the centrum. The total growth represents the sum of the growth at the lateral and medial ends of the ala, together with that at the lateral aspect of the centrum.

It is observed from Table VIII that there is a remarkable accordance between the actual and expected increments over a period of 199 days.

Now examining the pelvis as a whole it is seen that the width towards the back includes the joints between centrum and ala of the sacrum together with the sacro-iliac articulation; while in front the width includes only the symphysis.

The antero-posterior diameter includes the joint between the pubis and ilium at the acetabulum.

In Table IX the actual increase in measurement of the width and antero-posterior diameters over a period of 199 days is compared with the expected increment. The expected increment to the width behind consists of twice the total expected increment for half the width of the sacrum shown in the previous table. The amount of growth on the iliac side of the sacro-iliac articulation is small and can be neglected so far as width is concerned.

Table VIII. *Measurements in mm. of actual increase and expected increment of pelvic bones over a period of* 199 *days as described in text*

Pig no.	14	15	16	17	12	1	2	3	4	Increase
Age in days	80	91	108	126	140	169	197	225	279	
Difference in age in days		11	17	18	14	29	28	28	54	
Ilia										
Length, actual	84·0	85·0	87·0	98·0	101·0	101·0	110·0	115·0	123·0	39·0
Expected increment:										
Crest end		3·15	3·55	4·50	2·80	4·00	3·60	3·00	5·04	29·64
Acetabular end		1·12	0·92	1·30	0·90	1·40	1·00	0·80	1·12	8·56
Total expected increment		4·27	4·47	5·80	3·70	5·40	4·60	3·80	6·16	38·20
Ischia										
Length, actual	65·0	65·0	67·0	75·0	75·0	73·0	80·0	84·0	97·0	32·0
Expected increment:										
Acetabular end		1·05	1·27	0·83	0·74	1·20	0·88	0·60	0·72	7·29
Tuberous end		2·25	2·25	3·00	1·94	3·72	3·60	3·00	2·96	22·72
Total expected increment		3·30	3·52	3·83	2·68	4·92	4·48	3·60	3·68	30·01
Pubes										
Length, actual	23·0	22·0	24·0	25·0	28·0	29·0	30·0	31·0	32·0	9·0
Expected increment:										
Acetabular end		0·33	0·25	0·20	0·14	0·28	0·24	0·24	0·32	2·0
Symphysial end		0·75	0·60	0·82	0·54	1·00	0·80	0·48	0·72	5·71
Total expected increment		1·08	0·85	1·02	0·68	1·28	1·04	0·72	1·04	7·71
Sacra										
Width from middle line	25·5	25·0	22·5	28·5	25·5	28·5	31·0	34·5	32·25	6·75
Total growth for half width per week	1·4	0·51	0·35	0·35	0·31	0·25	0·22	0·22	0·14	
Expected increment for half width		0·80	0·88	0·88	0·62	1·00	0·88	0·88	1·12	7·06

The increment to the width in front is the sum of the growth of the symphysial end of the two pubic bones.

The expected increment to the antero-posterior diameter consists of the sum of the new growth at the acetabular ends of the pubis and ilium.

Table IX. *Measurements in mm. of actual increase in the diameters of the pelvis compared with the expected increments*

				Expected increment	
	No. 14	No. 4	Actual increase	Behind	In front
Width	50·2	63	12·8	13·50	11·76
Antero-posterior	51·3	77·0	25·7	10·57	

These measurements and calculations show that the growth in width of the pelvis is fairly accounted for; but there is a large hiatus between the actual and expected increase in the antero-posterior diameter (25·7 − 10·57 = 15·13 mm.).

The index of the pelvic brim already stated shows this antero-posterior diameter to increase faster in relation to the width.

Now the actual increase in length of the bones forming the pelvis has been fairly accounted for by the increments at each end; so that this apparent outstanding difference of 15·13 mm. between actual and expected antero-posterior diameter draws attention to the sacro-iliac articulation.

The distance between the ventral limit of the sacro-iliac articulation to the crest of the ilium measured in the same plane as the length of the ilium is in No. 14, 41·0 mm., and in No. 4, 56·5 mm., making a difference of 15·5 mm. The new bone added to the crest of the ilium has been noted in Table VIII to amount to 29·64 mm., which might be the expected difference between the last measurements. The difference, between actual and expected differences, amounts to 14·14 mm., and this helps to explain the deficit (15·13 mm.) between actual and expected antero-posterior diameters of the pelvic brim, and, together with the previous observation that absorption is taking place at the cranial margin of the sciatic notch, indicates that the sacro-iliac articulation travels cranially at approximately the rate of 14·14 mm. in 199 days.

CLINICAL APPLICATION

It would appear, from the foregoing description of the "Growth of the Pelvis", that those abnormalities of the pelvis not caused by disease would fall into two classes:

(1) Those due to abnormal end growth of the pelvic bones, such as early and delayed osseous union of the parts of the innominate bone at the acetabulum. An early union of these parts of the innominate might account for the simple flat pelvis when the antero-posterior diameter is diminished.

(2) Those due to failure of the sacro-iliac articulation to move towards the crest of the ilium. This would manifest itself by an unusual distance between the joint and the crest of the ilium together with a decrease in the antero-posterior diameter. Such a condition could be unilateral and might account for "Naegeles Oblique Pelvis" where the end growth of the ilium appears to be normal.

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DISSECTIONS OF NEPHRONS FROM THE HUMAN KIDNEY

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MUCH of our exact knowledge of the structure, varieties and arrangement of the nephrons in the kidney of Man and of several lower animals is based on the monumental work of Peter (1909). He first applied and perfected for this purpose the method of maceration in strong hydrochloric acid which softens and removes the interstitial substance leaving the glomeruli and epithelial structures more or less intact. In this way he was able to separate large portions of many nephrons and occasional complete structures, and so to obtain measurements of the various segments and accurate data as to their positions and relationships in the kidney. He remarked on the great difficulty of securing permanent preparations of these delicate objects and on the relative rarity of obtaining suitably fresh human material for dissection. Huber (1911) later discussed certain modifications in the technique of maceration and applied the method with great success to kidneys of freshly killed rabbits, cats, dogs, guinea-pigs and rats. He first injected 75 per cent. hydrochloric acid into the renal arteries, then divided the organs into several portions and allowed maceration in strong acid to proceed for 3 or 4 hours. After subsequent washing in water the tissues were stained in bulk with Mayer's haemalum, washed, alkalinised, and finally submitted to dissection with very fine needles under the microscope. By this procedure Huber isolated a large number of complete nephrons which could be drawn to scale and measured, and several beautiful figures of these preparations are shown in his communications. Huber found difficulty in securing similar results from human kidneys, and in his well-known article on renal tubules (1932) he makes no reference to any later success with human material. Traut's (1923) studies of human kidneys were based upon specimens macerated in 50 per cent. hydrochloric acid for 8–12 hours, usually after the tubules had been injected from the ureteral aspect with ferrocyanide, so as to give the effect of a Berlin blue mass in the lumina: kidneys of foetus, children and adults were examined. His main conclusion was that the kidney could be subdivided into structural units composed of 140–180 nephrons which were connected, by successively uniting branches of collecting tubules, downwards to a single collecting duct of the eighth order of division: such units receive their blood supply from their periphery. He claimed also to have found it easy "to remove whole renal tubules or groups of two or three

still in their original positions and connected to the ducts", but he gives no measurements of any of the segments or of complete nephrons. As the dimensions of the single uriniferous tubules derived from each tuft appear to carry great significance in any attempt that may be made to realise the conditions under which urine is elaborated, much further work on this point is probably desirable. An opportunity to follow this up over a short period has recently presented itself, and the results obtained in semi-permanent mounting, measurement, and photographic representation of human nephrons may be deemed worthy of record.

TECHNIQUE

In attempting to obtain preparations of human tubules many valuable hints have been gathered from the works of Peter and of Huber, but the method of preliminary injection of arteries employed by the latter has not so far proved completely advantageous, though this may be owing to insufficient experience. The method which has proved most successful so far in our hands is as follows: A kidney as fresh as possible is cleared of fatty tissue, but the fibrous capsule is left intact. A half of the organ is placed in about three times its volume of 75 per cent. hydrochloric acid for 20 hours and then allowed to remain in 5 per cent. acid for 2 or 3 days. During this time the tissue swells and becomes somewhat transparent. The acid is then carefully washed out of the container by a stream of running water and the tissue allowed to remain in water for half an hour. Wedge-shaped portions of kidney, including cortex and corresponding medulla, are then cut off with the edge of a thin glass slide and transferred to a large Petri dish half-filled with fresh tap water. Dissection can be carried out at once or at any time in the following week. The addition of 0·5 per cent. formalin has been found to harden the tubules slightly and enable them to be kept and dissected even after a month. No staining of the tissues has been attempted. Dissection has been carried out with a single finely drawn out glass needle under a dissecting microscope at a magnification of ×10. The process of dissection consists in the slow and careful following up of a single tubule with the glass needle and gently separating it bit by bit from the other tubules to which it may be lightly adherent. In working the needle point between adherent segments, breakages naturally occur very easily. The narrow limbs of the loop present especial difficulty, and particularly those embedded in the denser connective tissue of the medulla. It is impossible completely to straighten out the natural coils of the convoluted tubules. The attempt has generally been made to retain the natural adhesion between the upper end of the ascending limb of the tubule and its own glomerulus. Once a nephron is separated it is raised gently in the water with the needle and there is thrust under it a slide which has previously had a rectangular dam of vaseline applied on its upper surface. When the structure has settled down on the slide and been properly arranged by gentle movements with the needle, a suitable large cover-glass is lowered over it in the water and pressed down on the vaseline

until sealing is just completed. The whole preparation can then be removed from the water. The nephrons are thus enclosed in formolised water in a cell about 0·5 mm. in depth. Many of those mounted still remain in good preservation after six months.

Measurements can be carried out directly on the straight parts of the tubules by use of stage and eyepiece micrometers. In all instances, however, the preparations have also been photographed at magnifications of ×10 to ×20 and tracings made from prints of these with the aid of microscopic observations on the original slides. From the tracings, finally, the measurements of the various coiled segments have been obtained by following their midlines with a rotameter or map measurer and making allowance for the magnifications. As Huber has pointed out it is impossible to make an exact allowance for the upward and downward curves in pictures of the convoluted parts, and measurements of these will always be slightly underestimated.

The photography of the slightly brownish unstained tubules has been carried out with Winkel micro-luminars 35 and 50 mm., using Ilford process plates, backed, with a Wratten C filter (blue), to increase contrast.

ORIGINAL OBSERVATIONS

The cases from which dissections were obtained were as follows:

(1) Male, aet. 20 years (G.R.I. 15,385), died of acute meningitis at 3.45 a.m. on 3. v. 34. Post-mortem examination 7 hours later.

(2) Male, aet. 11 years (G.R.I. 15,426), died of tuberculous meningitis at 3.35 a.m. on 4. vi. 34. Post-mortem examination 6½ hours later.

(3) Male, aet. 10 years (R.H.S.C. 3944), died of acute enteritis at 7.35 a.m. on 13. vi. 34. Post-mortem examination 4 hours later.

The record of results falls into two parts, first a general account of the different types of nephron which corresponds in the main with the fuller descriptions by Peter, and secondly the measurements obtained from some complete or almost complete structures.

(*a*) The first type of nephron to be described starts from a glomerulus in the deep part of the cortex. In some kidneys these glomeruli are larger than those situated peripherally, though in the kidneys dissected by Peter this difference was not found. Starting from the tuft the first convoluted tubule, which appears greyish brown and granular, winds towards the periphery of the kidney in a closely packed mass, not mingling with other tubules. After several main coils with innumerable fine subsidiary turnings, it returns near to its own tuft and then extends almost straight towards the medulla in a ray, along with similar segments of other tubules. It gradually narrows at the edge of the cortex to be succeeded by the narrow limb of the loop. This is distinctively clear and transparent and extends for a variable but often considerable distance straight into the medulla, sometimes reaching nearly to the papilla. It then bends, forming the actual loop of Henle and returns straight towards the boundary zone, changing to broad ascending limb in a zone of

about 3 mm. width, short of the margin of the cortex. This broad limb is again granular and cloudy compared with the narrow one. It passes straight to the glomerulus of the same nephron (Plate I, fig. 1) and becomes fairly firmly attached to one of the arterioles, according to Peter, always the efferent vessel. From this point the tubule exhibits several sharp bends, forming the characteristic portion described by Peter as the "Zwischenstück". This short segment, which can also be regarded as the commencement of the distal or second convoluted tubule, is the only part of the latter which lies near the tuft. Thence it passes on as the second convoluted tubule in a zigzag course between masses of first convoluted tubules to join another structure of the same type before ending in a collecting tubule (Plate I, fig. 2). The opinion of Traut (1923, p. 117) that the distal convolutions lie in closest apposition to the glomerulus and that the proximal convolutions lie for the most part superimposed on those of the distal portion is quite contrary to our observations, as it is to the descriptions by Peter. Judging from our measurements and photographs, which reveal the preponderance in bulk of the proximal tubules in all instances, Traut's less complete macerations have prevented him from distinguishing the distal from the proximal segments. His conclusion also does not appear to be borne out by his fig. 12, which clearly shows the distal tubule ascending past the tuft towards the periphery. The cells in the Zwischenstück are the clearest in this part of the tubule, while the middle part of the second convoluted tubule is darkest and most granular. The collecting tubules further on are distinctively clear in appearance. While many of these deep nephrons have been traced, it has not been found possible so far to separate one intact owing to the difficulty of extracting the thin limbs from the dense connective tissue of the medulla.

(*b*) Nephrons of the second type arise from tufts in the middle or outer zone of the cortex. They differ from the first chiefly in that the narrow limb changes to the broad while still descending, so that the bend of the loop is formed by the latter (Plate II, fig. 1). The bends occur in the outermost zone of medulla or in the medullary ray in the cortex. The narrow limb is of very variable length and sometimes measures only a few microns (Plate II, fig. 2).

(*c*) In some parts of the cortex, usually opposite medullary rays, there occur groups of short nephrons which possess no narrow limb (Plate II, fig. 3). The straight descending part of the first convoluted tubule joins the broad limb directly. The loop of Henle formed by the latter often shows a spiral turn. The broad limbs are shorter than in (*a*) and (*b*), but the second convoluted tubules are distinct and long. Structures of this type occur in closely associated groups and are difficult to separate. They have not been identified in all the kidneys examined.

The second convoluted tubules of the peripheral nephrons (*b*) and (*c*) appear to change directly to collecting tubules, whereas those of the deep nephrons join together before entering these. Considerable segments of collecting tubules have been separated, but no complete ones. A large portion

is shown in Plate III, fig. 1, with a nephron attached. The larger ducts of Bellini appear to break down rapidly after death.

The measurements obtained from complete or almost complete nephrons and from complete segments of some others are given in Table I.

Table I. *Lengths of tubules in millimetres.*

Case	Tubule	1st con. tub.	Narrow limb	Broad limb	2nd con. tub.	Total length
		(*a*) Complete or almost complete nephrons.				
1	A	20·65	5·0	14·53	1·875*	42·055
	B	20·72	5·6	15·0	2·34*	43·66
	G	19·06	3·75	13·75	3·437	39·997
	H	14·14	None	6·09	4·21	24·44
	L	23·12	1·66	10·62	1·79*	37·19
2	A,*a*	7·285	3·12	7·5	1·875	19·78
	A,*b*	8·44	2·7	7·08	2·34	20·56
3	B	8·7	3·3	9·1	1·7*	22·8
	C	11·6	3·3	9·58	1·56*	26·04
	F	11·56	3·125	9·375	3·75	27·81
	G	11·25	5·3	10·625	3·1	30·275
		(*b*) Complete segments only.				
1	C	18·9	—	—	—	—
	D	21·718	7·187	17·65	—	—
	F	21·875	—	—	6·32	—
	F,*a*	—	—	—	3·43	—
	I	17·81	13·875	—	—	—
2	B	8·75	—	7·5	2·5	—
Peter's av. figures (adults) (p. 197)		14·0	2–10	9·0	4–6	30–38

* 2nd con. tub. not quite complete.

The measurements of length vary somewhat, but those obtained from case 1 are comparable in size and range of variation with those given for the secretory parts of the tubules by Peter. 1 H, which is relatively short, is of type (*c*) with no narrow limb. Tubules 1 D and I are of type (*a*), and show the great length of the narrow limb. Peter estimated the length of these long narrow limbs at 4·5–16 mm. with an average of 10 mm. The rest of the tubules are of type (*b*) with narrow limbs very variable, 1·66–5·6 mm.

In the younger subjects 2 and 3 the tubules are distinctly shorter than in the adult but show the same general conformation. A point of pathological interest noted in the dissections was that in two of the cases a few tubules contained blood and accordingly stood out as prominent objects (Plate III, fig. 2). The even distribution of the blood in these first convoluted tubules from the glomerulus or near it downwards was in keeping with the view commonly accepted that tubular haemorrhages arise from the tufts.

A few measurements of tubule diameters are given in Table II. These are much greater than corresponding measurements given by Peter and may indicate some swelling of the material, though the procedure followed in preparation has been similar to his.

One main effect of this work is to emphasise again the great length of the secretory parts of the renal tubules, often about 4 cm. in the adult, compared

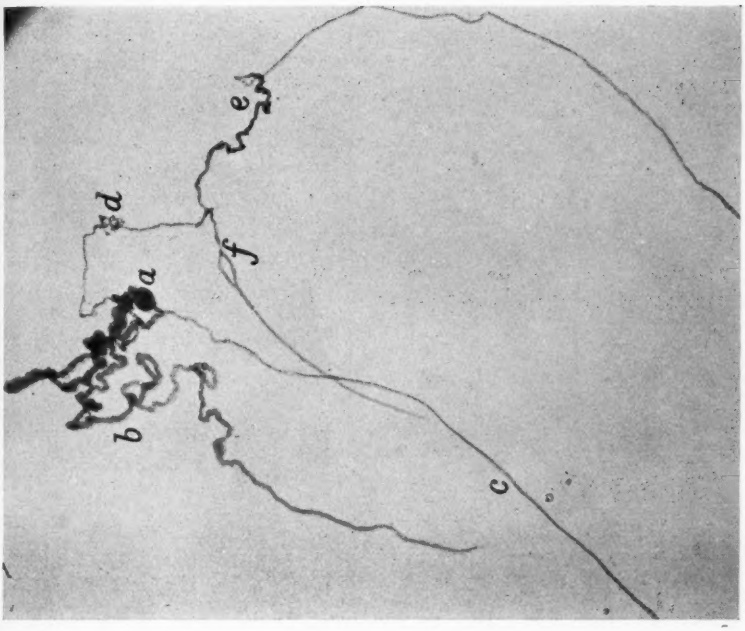

Fig. 2.

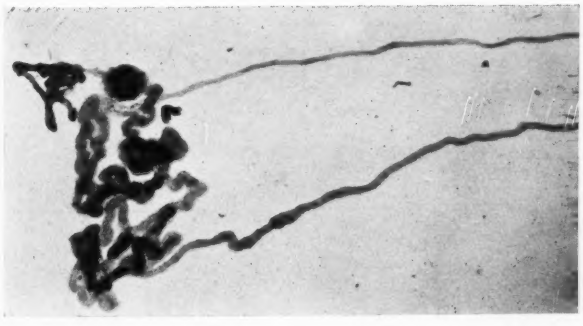

Fig. 1.

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Fig. 3.

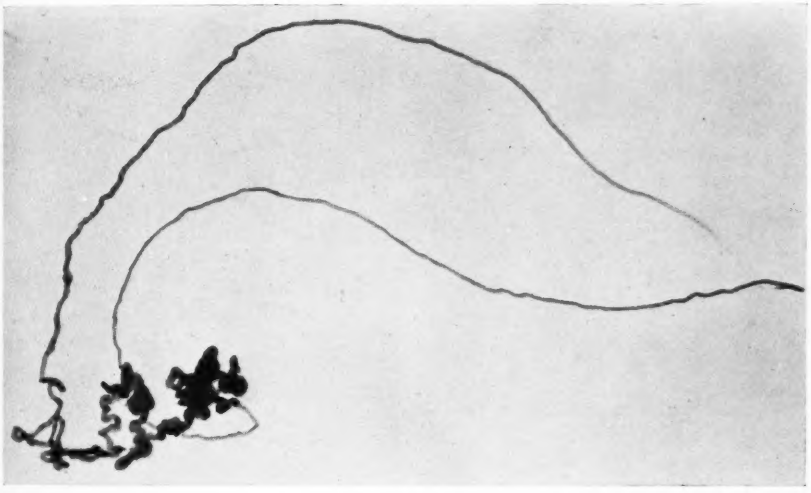

Fig. 2.

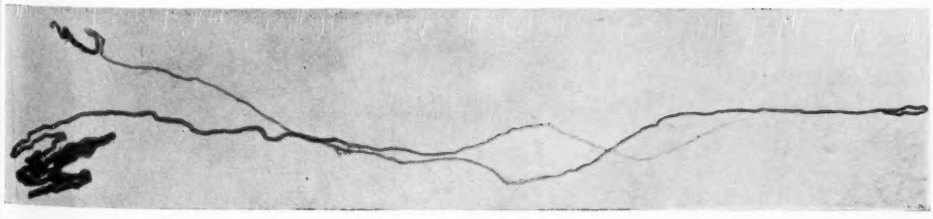

Fig. 1.

HSI-CHING PAI—NEPHRONS FROM THE HUMAN KIDNEY

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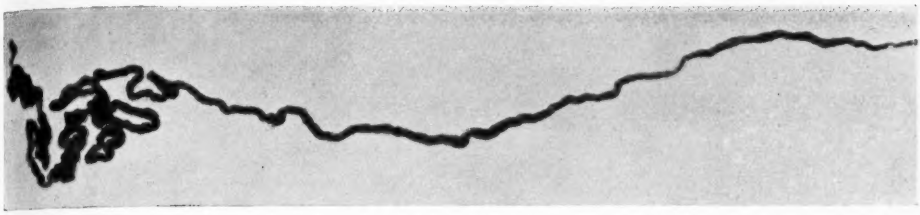

Fig. 2.

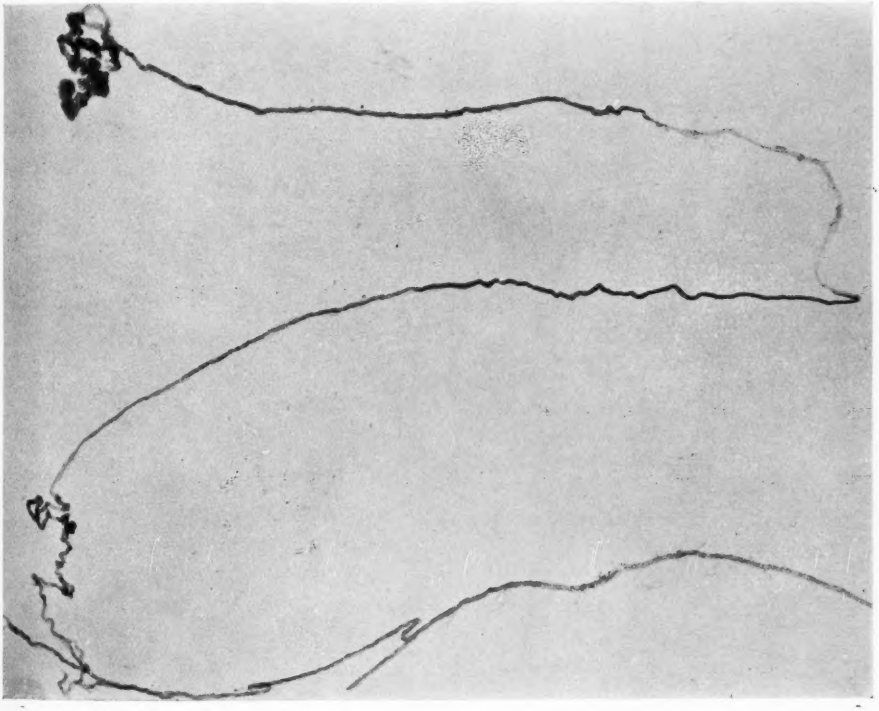

Fig. 1.

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with their diameter, a feature which cannot fail to have significance in attempts to interpret renal functioning.

Table II. *Diameters of glomeruli and tubules in microns.*

Case	Tubule	Glomerulus	1st con. tub. Coiled part	1st con. tub. Straight part	Narrow limb	Broad limb	2nd con. tub.
1	A	300	79·7	72–51	30	45–51	60
	B	336–276	75·0	75–57	28	45–53	51
Peter's av. figures		152–159	57		15	30	41

In conclusion I express my indebtedness to the Management of Glasgow Royal Infirmary for laboratory accommodation, and to Prof. Shaw Dunn for valuable suggestions and assistance with photography.

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EXPLANATION OF PLATES I–III

Plate I

Fig. 1. Peripheral part of a nephron in case 1. The first convoluted tubule is seen to start from the glomerulus on the right and after many windings to descend towards the medulla on the left. The broad ascending limb comes up on the right to the tuft, where it is attached, then passes above the latter as second convoluted tubule showing several zigzag bends. ×20.

Fig. 2. Junction of two second convoluted tubules of type (*a*) nephrons. The glomerulus *a* gives off first convoluted tubule *b* which sends down its descending part to end in a break of the narrow limb. The broad ascending limb *c* of the same nephron ascends from below and passes the glomerulus to form second convoluted tubule *d*. The latter joins a similar tubule *e* and the united tubule enters a collecting tubule *f*. ×10.

Plate II

Fig. 1. Complete nephron (case 1 A) of type (*b*): shows a fairly long narrow limb, and the turn of the loop formed by broad limb. ×10.

Fig. 2. Complete nephron (case 1 L) with short narrow limb: type (*b*). ×10.

Fig. 3. Complete nephron (case 1 H) with no narrow limb: type (*c*). The broad ascending limb and second convoluted tubule have been drawn downwards. ×10.

Plate III

Fig. 1. Complete nephron (case 3 F) attached to collecting tubule. The latter joins with others to form a larger one which receives further branches. ×15.

Fig. 2. First convoluted tubule (case 1 C) filled with haemorrhage. The tuft is detached. ×15.

ON THE ANATOMY OF INTERCOSTAL SPACES IN MAN AND CERTAIN OTHER MAMMALS[1]

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The standard description of the anatomy of the intercostal space has been discussed by Stibbe in a paper recently published in this *Journal* (2,3).

Prof. Walmsley in 1916 (1) showed that the intercostal nerves do not lie in the plane between the internal and external intercostal muscles but deep to the internal intercostal, and that they are separated from the pleura by a deeper musculo-fascial plane consisting of subcostal, intercostal and transversus thoracis muscles from behind forwards.

According to Davies, Gladstone and Stibbe (3) there are four musculo-fascial planes in each space and in each space the main nerve lies with a collateral nerve deep to the internal intercostal.

As the above paper effected a change in the teaching of the anatomy of intercostal space, we carried out the following investigations on human as well as on certain other Mammalian intercostal spaces.

DISSECTION OF HUMAN INTERCOSTAL SPACES

Sixty thoraces of different ages were dissected. From some of them the intercostal spaces were cut out *en bloc* to facilitate dissection; in others the thoracic wall was dissected as a whole. In the case of the foetuses microscopic sections were made to locate the muscular planes and the nerves.

The results of our dissection were as follows:

I. *Intercostal muscles* (fig. 1)

The muscles in each intercostal space are five in number, arranged in three planes from without inwards:

(1) External intercostal in the outer plane.

(2) Internal intercostal in the intermediate plane.

(3) The three muscles, subcostal posteriorly, intercostal intermediately, transversus thoracis anteriorly, form the innermost plane.

The external intercostal muscle and its continuation, the anterior intercostal membrane, agree with the usual description.

The internal intercostal takes origin by thin tendinous slips from the upper

[1] The expenses incurred in connection with this investigation were borne by a grant from Kunwar Indrajit Singh Research Fund.

lip as well as from the floor of the subcostal groove. The posterior intercostal membrane is the direct continuation of this muscle and posteriorly becomes continuous with the anterior costo-transverse ligament.

The intercostal muscle takes origin by thin tendinous fibres from the upper lip of the subcostal groove and at places from the inner surface of the upper rib. At its insertion below, it fuses with the fibres of the internal intercostal and thus has a conjoint insertion on the inner lip of the upper border of the lower rib.

The transversus thoracis is in conformity with the usual description.

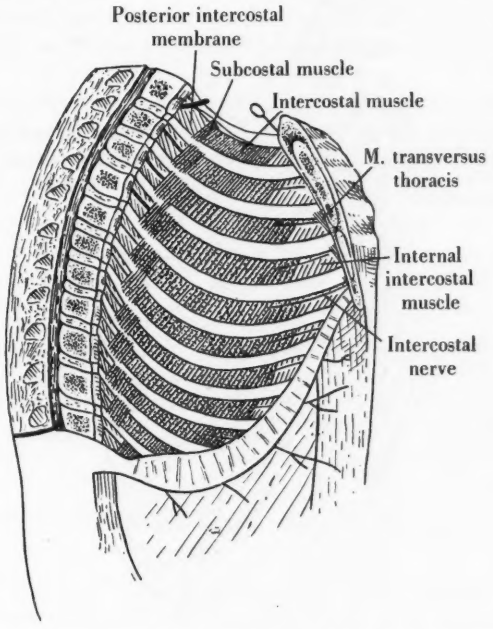


Fig. 1. Human thorax after removal of parietal pleura (post part).

The endo-thoracic fascia, which extends between the muscles of the third plane, lines the thoracic cavity on the external surface of the parietal pleura and has the following relations:

Posteriorly in the middle line in front of the vertebral column it becomes continuous with the fascia of the opposite side. When traced forwards it splits to enclose the sub- and intercostal muscles. At the anterior border of the intercostal muscle the fascia covers the inner surface of the internal intercostal muscle and splits again to enclose the transversus thoracis muscle. It fuses with the periosteum of the sternum in the middle line anteriorly, where it becomes continuous with the fascia of the opposite side.

THE INTERCOSTAL NERVES AND ITS BRANCHES

With Walmsley and Stibbe we agree that the main intercostal nerve does not lie between the external and internal intercostal but lies deep to the latter muscle.

The collateral nerve, as described by Stibbe, was found only in 130 out of 1386 spaces dissected by us, i.e. in approximately 10 per cent. of the spaces. It is therefore not a constant feature in the arrangement of the intercostal nerves.

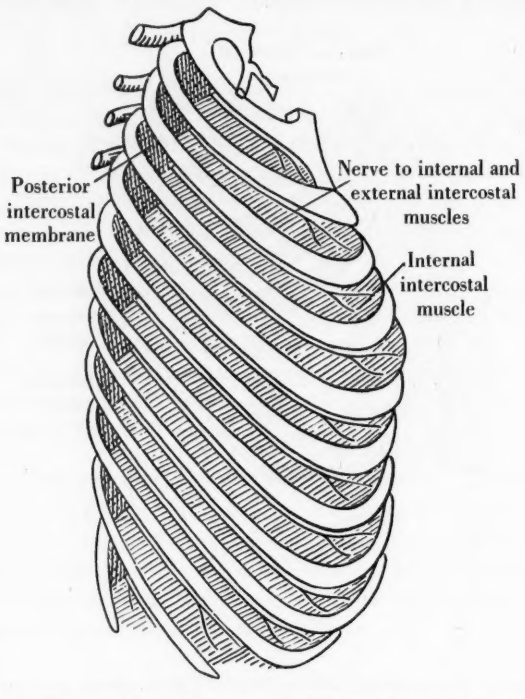


Fig. 2. Human thorax after removal of external intercostal muscle and anterior intercostal membrane.

Both in man and animals in most of the spaces a branch of the main nerve (fig. 2) passes outwards for a short distance on the posterior intercostal membrane, then pierces the internal intercostal muscle near its upper border and about half an inch anterior to its posterior border, and then comes to lie between the external and internal intercostal muscles. This branch is found just below the upper rib of each space between the two muscles. It lies in contact with the inner aspect of external intercostal, and supplies the external and internal intercostal muscles.

DISSECTION OF INTERCOSTAL SPACES IN LOWER ANIMALS

The animals dissected for the above purpose were the dog, cat, rabbit, monkey, goat and lamb.

In the dog, cat, rabbit and monkey, the results of the dissection were as follows:

(1) Each intercostal space contains five muscles arranged in three planes exactly as in man. The subcostal muscle is poorly developed. The transversus thoracis is well developed and its fibres run in a horizontal direction from the sternum to costal cartilages.

(2) The posterior border of the internal intercostal reaches quite close to the bodies of the vertebrae so that the posterior intercostal membrane is very narrow.

(3) The arrangement of the intercostal nerve and its branches resembles very closely that of man, i.e. the main intercostal nerve lies between the internal intercostal and the innermost plane formed by the musculo-fascial layer. The

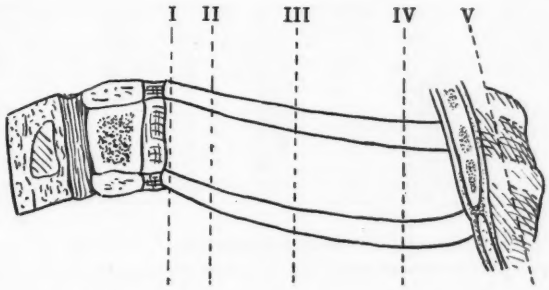


Fig. 3. Sketch showing levels of cross sections for fig. 4.

main nerve can be seen after the removal of the parietal pleura between the intercostal and transversus thoracis, a gap where the nerve is separated from the pleura only by the endothoracic fascia.

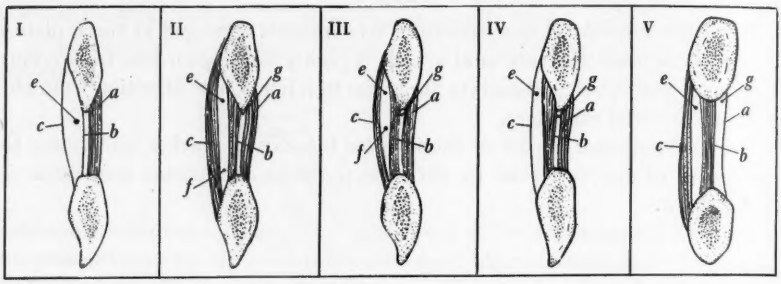
(4) The collateral branch is absent in every space.

(5) The long thin muscular branch which was seen in human spaces between the external and internal intercostal is present in every case. The position is just below the lower border of the upper rib in each space more adherent to external intercostal than internal intercostal.

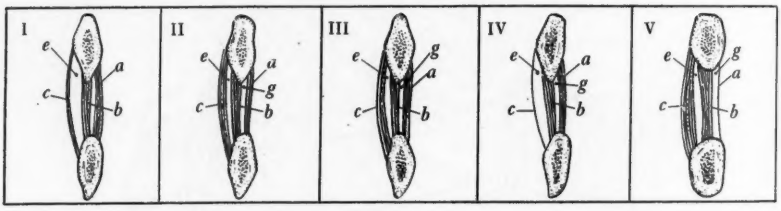
In the goat and lamb the *intercostal muscle is altogether absent.* The intercostal nerve is separated from the parietal pleura by the endothoracic fascia only. *As soon as the parietal pleura is removed the nerves are seen shining through the fascia.* The subcostal muscle is also absent in the upper spaces. The transversus thoracis, a very well-developed muscle, runs horizontally from the sternum to the costal cartilages. There is a strong ligamentous band on the

inner side of this muscle running along the lateral side of the sternum as if to keep the muscle in position. The band fuses at the inner surface of the manubrium sterni with periosteum and lower down with the costal cartilages of the 8th, 9th and 10th ribs.

1. Human.



2. Mammals, group A.



3. Mammals, group B.

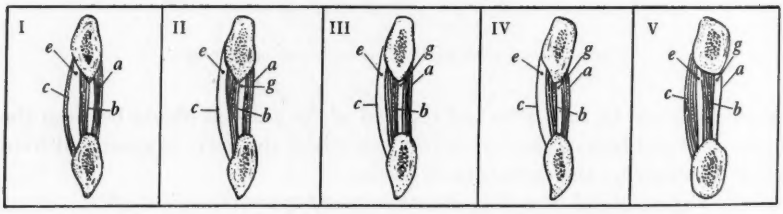


Fig. 4. Diagrammatic comparative chart of cross sections of intercostal spaces according to fig. 3.

a. Muscles of first layer: external intercostal muscle and the anterior intercostal membrane (a_1).
b. Muscles of second layer: internal intercostal muscle and the posterior intercostal membrane (b_1).
c. Muscles of third layer: *c* 1, transversus thoracis; *c* 2, intercostal; *c* 3, subcostal.
d. Endothoracic fascia.
e. Main intercostal nerve.
f. Collateral nerve.
g. The muscular branch.

SUMMARY

A. Intercostal spaces from sixty human thoraces of different ages were dissected and the following is the result of the investigation:

(1) There are five muscles in each space arranged in three planes:

(*a*) External intercostal.

(*b*) Internal intercostal.

(*c*) Subcostal, intercostal and transversus thoracis connected with one another by the endothoracic fascia.

(2) The subcostal and intercostal lie in the same plane and connect with each other.

(3) The main intercostal nerve lies between the internal intercostal and the innermost muscular and fibrous plane.

(4) A big collateral nerve is given off by the main nerve in some spaces only and occupies the same inter-muscular plane as the main nerve.

(5) Between the external and internal intercostal muscles there is present a thin long muscular branch which extends up to the side of the sternum and supplies the external and internal intercostal muscles.

(6) The posterior intercostal membrane is continuous with the internal intercostal muscle anteriorly and anterior costo-transverse ligament posteriorly.

B. The dissection of the intercostal spaces of dog, cat, rabbit, monkey, goat and lamb discloses the following:

(1) The arrangement of the muscular planes is in general the same as in the human being.

(2) The intercostal nerves occupy the same plane as in man.

(3) The collateral nerve is absent in every case.

(4) A long thin nerve between the external and internal intercostal muscle is always present.

Lastly we take this opportunity of expressing our grateful thanks to Raja Sir Harnam Singh, the donor of the Captain Kunwar Indrajit Singh Scholarship, which enabled us to carry out this work.

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A "SEXUAL SKIN" IN A MARMOSET

By A. E. RUSSELL and S. ZUCKERMAN[1] (*Beit Memorial Research Fellow*)

From the Department of Human Anatomy, Oxford, and the Department of Physiology, Yale University School of Medicine

Cyclical variation in the conformation of the circumgenital area, such as occurs in many species of Old World Primates, has never been reported in South American monkeys. The present paper gives a description of the ano-genital region in an adult marmoset in which such changes are reported to have occurred. The identification of the specimen, which was bought for experimental purposes and used in a study of cortical function, is unfortunately not quite certain. The general characters of the carcass are undoubtedly those of *Hapale jacchus*, the common marmoset, but the specimen also shows resemblances in the colour of the hair of the head and thoracic regions to the variety of this species which goes by the name of *H. albicollis* (Plate I, fig. 1).

Specific details of the degree of fluctuation in size of the circumgenital area exhibited by the animal, and of the periodicity of the fluctuation, are not available. The turgid state of the circumgenital tissues in the fixed specimen suggests, however, that there was considerable scope for such fluctuation (Plate I, fig. 2, shows a photograph of the swelling when it is said to have been at its maximum size).

The fact that the circumgenital pad—or "sexual skin"—is pedunculated is in itself sufficient reason for the present detailed report. No such condition has previously been described in the Hapalidae. Moreover, while the glands of the well-known perineal pad of the marmoset have been investigated (Wislocki, 1930), to our knowledge attention has not previously been paid to the muscles of the region.

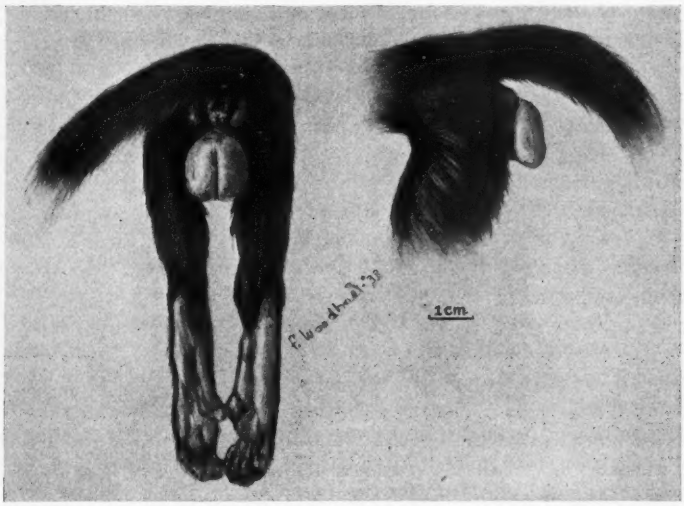
Text-figs. 1 *a* and *b* provide an end-on and a lateral view of the perineal swelling drawn to scale, and practically life size. The swelling extends ventrally to overlap the symphysis pubis. Dorsally it terminates in front of the anus. The pedicle is much smaller, both laterally and ventro-dorsally, and extends from the lower margin of the symphysis pubis back towards the anus, which is on a level with the ischial tuberosities. The ventral two-thirds of the swelling are cleft by the urogenital sinus. The swelling is smooth and somewhat tense. The clitoris can be seen at the ventral limit of the cleft.

Text-fig. 2 *b* is a ventral view of the swelling, uterus, ovaries and bladder dissected away from the body; the upper part of the bladder has been removed

[1] At the start of this study a Rockefeller Research Fellow in the Yale University School of Medicine.

and a probe passed through the urethra and urogenital sinus. The ovaries are relatively large, but they give no indication of recent ovulation. The uterus is unilocular and small.

Text-fig. 2 *a* provides a dorsal view of the specimen, with the dorsal wall of the vagina and urogenital sinus removed. The probe traversing the vaginal opening of the urethra can be seen passing behind a small bridge of tissue uniting the two halves of the vulval swelling at the dorsal limit of the urogenital cleft. Longitudinal vaginal rugae can be seen just above the urethral papilla; they stop abruptly at a fold of mucosa which arches on each side of the urethral opening. The supra-urethral vaginal mucosa is not as smooth as the mucosa below the urethral opening.



Text-figs. 1 *a* and *b*.

From the studies of Klaatsch (1892) and Bolk (1907), it is plain that the area of swelling is limited to what are the homologues of the labia majora.

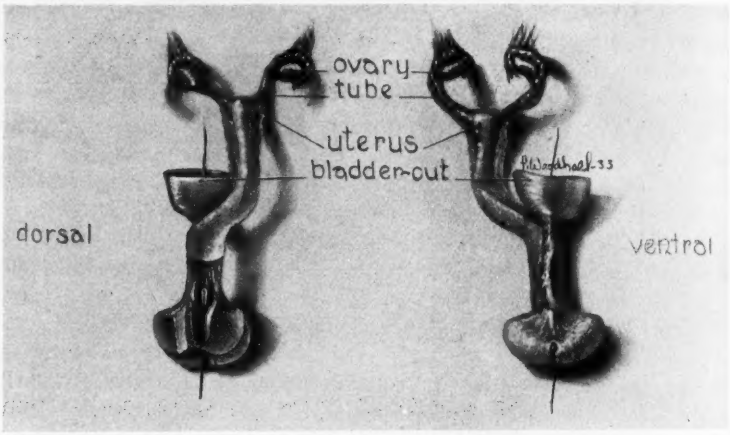
The pedunculated circumgenital swelling was separated from the upper part of the urogenital tract just below the urethral opening, and was serially sectioned in as near a horizontal plane as could be achieved, sections being stained with Mayer's haemalum and eosin. The part of the vagina immediately above was also serially sectioned.

The urogenital cleft. The urogenital sinus is a continuation and ventral expansion of the vaginal lumen. Its anterior wall is not as long as the posterior, which is continuous in a straight line with that of the vagina. There is no trace of a hymen. The line of junction between vagina proper and urogenital sinus may be regarded as the level of the urethral papilla. The swelling is limited to

the tissues below this level, which is situated about 6–7 mm. from the most dependent part of the swelling. Within about 2 mm. of its origin, the anterior expansion has extended ventrally sufficiently far to divide the genital swelling into two lobes (labia majora); from this level downwards these lobes are connected by only a bridge of tissue dorsally.

The clitoris and the minute folds of the labia minora are situated at the ventral limit of the ventral expansion. Lateral vaginal recesses are continued downwards as grooves which fade out at the level of the labia minora. These grooves divide the urogenital sinus into ventral and dorsal parts.

The epithelium. The mucosa of the vagina proper is irregularly corrugated owing to the presence of numerous mucosal papillae. The epithelium varies in thickness, being about four or five cells thick over the surface of the papillae,



Text-figs. 2*a* and *b*.

and about seven to twelve cells thick in the depressions between them. The irregularity of the mucosa is most marked at the junction of the vaginal and urethral mucous membrane, finger-like epithelial processes extending into the submucosal connective tissue. There is no evidence of either mucification or cornification.

The epithelium of the ventral part of the urogenital cleft remains similar in character to that of the true vagina as low down as the level of the labia minora, whose epithelium is thicker, squamous and keratinised.

The epithelium of the posterior part of the urogenital sinus is smooth, and thinner than that of the vagina. Its general appearance suggests considerable stretching.

The epithelium of the surface of the swelling is low and stratified. Its superficial layers are cornified, and in many places in process of desquamation.

Glands opening into the vagina and urogenital sinus. (*a*) What may be termed a "urethral" group of glands lies in small bunches in the angle between the circular layer of involuntary muscle fibres of the urethra, and a more prominent mass of voluntary muscle fibres ("inferior longitudinal vaginal muscle") which arises from the subpubic arch and passes distally to encircle the urethra and vagina. The ducts of these glands open separately into the vaginal recesses on each side of the urethral papilla; no glands open directly into the terminal part of the urethra or on to the urethral papilla itself.

(*b*) A more compact and prominent mass of glands, broken up into several lobes, each with a separate duct, opens into the lateral vaginal recesses below the opening of the urethra, and into the grooves which are their downward continuation. These may be termed the vestibular glands. In all likelihood they are homologous with Bartholin's glands. Their acini lie both outside and within the voluntary muscle mass referred to above.

The urethral and vestibular glands have the same histological appearance. They are tubulo-racemose in type, with the usual epithelium, and are in an active phase of secretion. The ducts and some of the acini are greatly distended, and contain coagulated secretion.

Glands of the external genital swelling. Apart from the glands already discussed, there are numerous others opening on the surface of the swelling and its pedicle. These glands are concentrated ventrally both in the most dependent part of the swelling and at the base of the pedicle. Over the greater part of the swelling they are disposed in a single layer of discrete systems lying parallel to the surface, and about 1 mm. beneath the dermis. They are least numerous in the region of greatest swelling.

Histological study shows that the surface glands are of two types: (*a*) a superficial layer of holocrine sebaceous systems whose ducts discharge in association with hair follicles (most of which contain degenerate hairs) into depressions on the skin surface. These glands lie entirely outside the lateral glandular muscles (see below). (*b*) A deeper layer of apocrine tubular glands. These are separated from the superficial holocrine group by varying amounts of connective tissue and by fibres of the "lateral glandular muscle".

Each holocrine gland system is made up of a number of short tubular acini containing large, pale-staining, closely packed, polyhedral cells with central nuclei. The lumina of these acini are obliterated by cast off degenerate cells. The main excretory duct of each system is lined with stratified epithelium and opens into the surface depression of a hair follicle. Each gland system is enclosed in a thick fibrous tissue capsule.

There are fewer apocrine than sebaceous glands. Although their ducts actually do burrow through the more superficial holocrine glands, the two types of secretory systems are not combined to form composite and discrete glandular organs such as Wislocki found in *Oedipomidas geoffroyi*. It is conceivable that the separation of the holocrine and apocrine glands is partly due to the oedema of the subcutaneous tissues, but it must be noted that both the

tubular and sebaceous types of gland are far fewer in the present specimen than Wislocki found in the form he described.

The histological appearance of the apocrine glands is suggestive of intense secretory activity. Some of the acini are lined with tall columnar cells whose central cytoplasm is in process of extrusion. Others are greatly distended with the products of secretion, and are lined with low cuboidal cells. Many acini appear simply as greatly dilated empty cystic spaces lined with flattened epithelium. In some places smooth muscle fibres can be seen between the basement membrane and the epithelium.

The coiled ducts of these apocrine glandular systems are of varying length, depending on the degree of oedema of the tissues in which they lie, and, as noted above, they pass through the holocrine glands into whose main excretory ducts they open.

The muscles of the perineal swelling. Owing to the fact that the specimen was separated from the pelvis, previous to its microscopical preparation, the bony connections of its muscular constituents cannot be definitely determined. Their general direction suggests that they took origin from the medial borders of the inferior pubic rami. The pedicle of the swelling is very muscular and consists largely of distally directed muscular strands passing ventral and lateral to the vagina. Presumably they also passed dorsally, but this is one of the points that cannot be definitely established owing to the "trimming" the specimen received. The main bundles which can be distinguished in the swelling proper are as follows:

Lateral glandular muscles. These pass to the lateral side of the genital swelling, the most distal fibres reaching to within about 2 mm. of its most dependent part. The fibres are directed distally and superficially, with varying degrees of obliquity. Some pass almost to the ventral convexity of the genital swelling, but none reach to the midline in front. The most medial distribution of this muscle bundle occurs above the level at which the vagina expands into the urogenital cleft. In this region a thin layer of fibres extends on either side almost to the midline between the ventral wall of the vagina and the clitoris.

The fibres are striated, and they mostly end blindly in the connective tissue. Many of them, especially below, terminate among the apocrine glands and their ducts. The contraction of these muscle bundles would presumably:

(1) Pull the genital swelling dorsally, thus bringing the urogenital sinus into line with the main axis of the vagina.

(2) Compress the deeper apocrine glands.

(3) Open the urogenital cleft.

Vaginal sphincteric muscles. These clearly defined striated muscle bundles pass ventrally and medially from their posterior origin on the subpubic arch, and are disposed deeply on either side close to the vagina. None of the fibres reach below a level about 3 mm. from the most dependent part of the swelling, all being restricted to the region above the main dilatation of the urogenital

sinus. The fibres do not extend more than 5 mm. ventral to the vagina, and the ventral margins of the two bundles are separated by about 4 mm. The direction of the muscular bundles clearly indicates their sphincteric action.

Ventrally and horizontally disposed sphincteric fibres do not occur above a level about 6½ mm. from the lower surface of the genital swelling. In this region their place is taken by a layer of longitudinally and distally directed muscle fibres which arch around the ventral and lateral walls of the vagina somewhat medial to the uppermost horizontal sphincteric fibres. The lower ends of these longitudinal fibres appear to end abruptly in a region where they overlap slightly with the horizontal sphincteric muscle.

The inferior longitudinal muscle of the vagina. The upper limit of the longitudinal muscle of the lower part of the vagina is about 7½ mm. from the most dependent part of the genital swelling. The muscle is only about 2 mm. long, and constitutes a very thin band that encircles the vagina.

The erectile tissue of the swelling. The erectile tissue of the swelling is differentiated into (*a*) erectile tissue of the corpora cavernosa and clitoris, (*b*) the erectile tissue immediately underlying the epithelium of the vagina and urogenital sinus, and (*c*) the subcutaneous tissue generally.

(*a*) The corpora cavernosa can be readily followed from their osseous origin to their union ventrally in the clitoris. They have a well-defined fibrous tissue capsule, and present the usual histological picture.

(*b*) The erectile tissue of the urogenital sinus and vagina forms a clearly demarcated submucosal region, 1–2·5 mm. deep, recognisable to the naked eye throughout the part of the reproductive tract that was sectioned, including the part of the vagina above the urethral papilla. The erectile zone extends to within 1·5 mm. of the most dependent part of the swelling. The most vascular region lies immediately below the urethral papilla and the lowermost stratum in which vestibular glands occur. Many arterioles approach to the base of the mucosa, where they break up into terminal capillaries. Numerous endothelial-lined vascular spaces occur in the submucosa. Vascular channels cannot be seen in the epithelium itself.

(*c*) The general subcutaneous tissue may for purposes of description be regarded as erectile in nature, in the same way as can the subcutaneous tissue of the sexual skin of the Old World monkeys, which histologically it closely resembles. Its fibrous elements are widely dispersed by oedema and are hyaline in appearance. Vessels of the swelling appear to be evenly distributed between the subepithelial and deeper regions.

SUMMARY

A detailed description is given of the structure of a pedunculated circumgenital swelling in an adult female marmoset, which is stated by those who had charge of the animal during its life to have undergone cyclical periods of swelling similar to those manifested by many Old World Primates. The histological appearance of the swelling is sufficiently like that of a "sexual

skin" to encourage the experimental investigation of its possible control by female sex hormones.[1]

We wish to express our deep appreciation to Mrs Frances C. Woodhall for her interest and for the skill with which she executed the figures. We are also greatly indebted to Dr J. F. Fulton for the opportunity of studying the specimen.

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EXPLANATION OF PLATE I

Fig. 1. Photograph of the marmoset which forms the subject of this report.
Fig. 2. Photograph of the animal, taken from behind. The central white area is the swollen "sexual skin".
Fig. 3. Photomicrograph, showing the general subcutaneous tissue of the circumgenital swelling.
Fig. 4. Transverse section of the more caudal part of the swelling. Note the superficial glandular systems, and the erectile zone immediately beneath the epithelium of the urogenital sinus. The epithelial fold in the upper part of the section is the praeputium clitoridis.
Fig. 5. Transverse section of the swelling at a more cranial level. On either side of the vagina can be seen the sphincteric muscles.
Fig. 6. Vestibular gland opening into the urogenital sinus.
Fig. 7. The superficial glandular systems. Note the layer of "lateral glandular muscle" separating the external holocrine from the deeper apocrine glands.
Fig. 8. The ducts of the deeper apocrine glands are shown passing upwards to come into relation with the superficial holocrine glands.

[1] We have failed thus far to induce perineal swelling in young marmosets by means of oestrin, superficial glandular changes being the only external manifestation of the hormone's action. A report of this investigation will be published later.

Fig. 1.

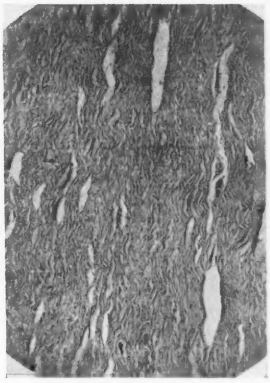

Fig. 3.

Fig. 2.

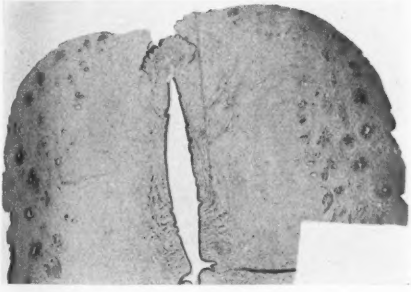

Fig. 4.

Fig. 5.

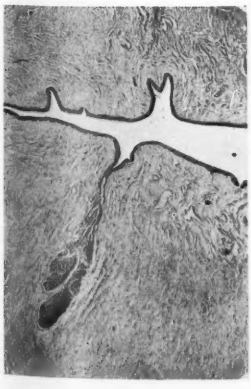

Fig. 6.

Fig. 7.

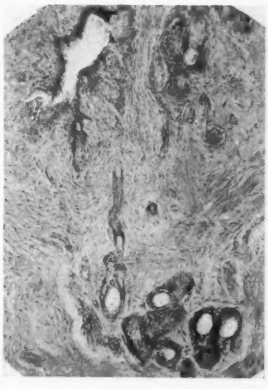

Fig. 8.

UNIV. OF MICH.

THE OVIDUCAL EPITHELIUM OF THE MOUSE

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INTRODUCTION

Allen (1) in his paper on the oestrous cycle in the mouse devotes some space to the consideration of certain changes which occur from time to time in the appearance of the epithelium of the inner ciliated portion, or ampulla, of the oviduct. He suggests that these changes are probably to be regarded as of degenerative significance, and concludes that they are in some way associated with the oestrous cycle, by which may be understood the spontaneous cyclical exhibition of certain phenomena, which can be produced at will by the injection of oestrin, and of which the most easily diagnosed is the keratinisation of the vagina. Allen speaks of a further description to be undertaken, but this does not seem to have been provided. The present investigation is intended to fill what seems to be a gap in the available descriptions of the relationship between the minute structure of the genitalia in this form and their functions. Hartmann's contribution to the symposium edited by Allen (2) may be consulted for a survey of the various views of the significance of the events in the oviducts, and the very useful paper by Novak and Everett (3) for a more detailed treatment of the human subject, and for an invaluable bibliography. Brambell (4) has described the development of the gonads without dealing exhaustively with the epithelia, and Agduhr (5), in his very complete description, deals particularly with the tubes, with little reference, however, to the oestrous cycle.

MATERIAL AND METHODS

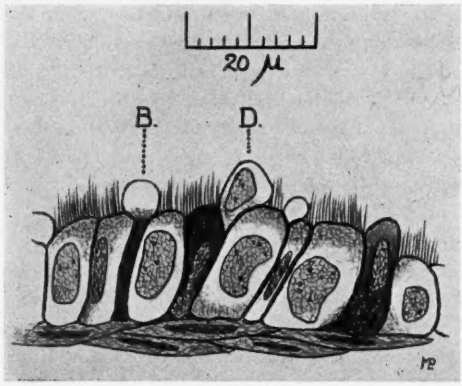
The ovaries of mice, whose vaginal smears had been taken for long enough to determine their condition, were fixed, the one in alcoholic Bouin and the other in Da Fano's fixative or in chrome-osmium. They were sectioned at between 4 and 10 μ and stained with Delafield's haematoxylin and eosin, iron haematoxylin, Mallory's connective tissue stain, and light green.

OBSERVATIONS

A section through the internal genitalia of a female mouse is shown in Plate I, fig. 1. The oviduct is divided into three parts which are easily differentiated from one another. At the inner end is the fimbriated funnel (*F*). This is in immediate connection with the ampulla (*Am.*). The epithelium of these parts is ciliated; that of the ampulla is shown in Plate I, fig. 3. This illustration is taken from a mouse in early oestrus. Nuclear displacement and apparent

extrusion are very clearly seen. The transition from this type of epithelium to that of the isthmus (*Ist.*) is abrupt. A single fold of the oviduct may indeed have one type on one side of it and the other on the other. The cell type of the isthmus is shown in Plate I, fig. 2. This is from a preparation to demonstrate the Golgi apparatus, which is particularly well defined in this tissue. These cells appear to be secretory, and sometimes contain fat, but they never show any sign of nuclear displacement.

In the embryo of about sixteen days from conception the whole of the Müllerian duct is lined with a comparatively undifferentiated columnar epithelium. In a young mouse two days after birth the epithelium at the inner end of the tube, which will become the funnel, is already thrown into the folds

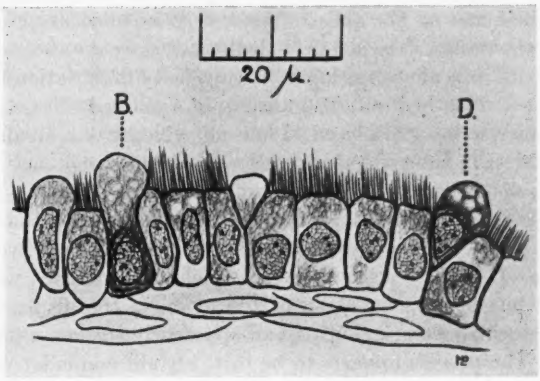


Text-fig. 1. Epithelium lining the ampulla of a female mouse six days old.

typical of this part in the adult. At four days the arrangement in the ampulla and funnel is practically that of a full-grown mouse, except that the ciliation is less complete. The phenomenon of nuclear extrusion, noted in particular by Allen (1), is well advanced, and can be seen in all its stages in many places. The nuclei which appear to be extruded belong to certain smaller, darker cells, which are to be seen, from the earliest stages, among the large clear ones, most plainly after osmium fixation. From what follows it seems probable that these are cells which are destined to remain unciliated. Text-fig. 1 shows an enlarged view of some cells from the ampulla of a mouse six days after birth fixed in this way. It will be seen that all the types of cell, and all the typical processes which have been described by previous authors (1, 2, 3, 6, 7) in the adult (text-fig. 2), are clearly shown here. This at once suggests that these phenomena are not primarily those of the oestrous cycle at all.

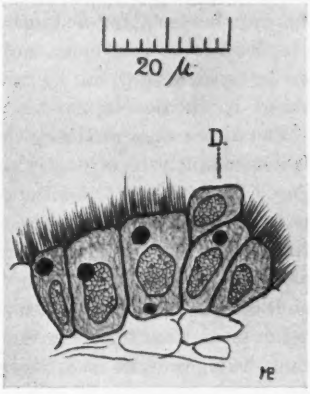
Text-fig. 3 shows the presence of obvious secretion in ciliated cells. It has been held that the secretion of this part is restricted to the non-ciliated cells. This I cannot confirm. A ciliated cell is shown here which has apparently just

discharged a drop of secretion through a break in its membrane without losing its cilia. I have been unable, in common with the authors quoted by Novak and Everett, to determine with certainty the nature of the secretion. It does



Text-fig. 2. Epithelium lining the ampulla of an adult female mouse at late met-oestrus.

Text-fig. 3



Text-fig. 4

Text-fig. 3. Epithelium lining the ampulla of an adult female mouse, at di-oestrus, showing secretion by ciliated cells.

Text-fig. 4. Epithelium lining the ampulla of an adult female mouse, at met-oestrus, showing fat globules in ciliated cells.

not appear to be mucin. The vacuoles sometimes attain very great size. Fat globules in ciliated cells are shown in text-fig. 4.

The ciliated cells vary considerably in width. They are usually large and clear, though occasionally small and dense. This presumably has some connection with the difference between the stages of secretory activity in which

they happen to have been fixed. They vary in height, but not regularly, nor on a very striking scale. I have measured the heights of ten cells in each of twenty-five mice in all stages of the oestrous cycle, and I find that the average, reckoning all the fixatives together, is about 13 μ, the lowest being 11·4 μ and the highest 15·9 μ. The tallest found were in mice at pro-oestrus and oestrus, but the results were not very significant, since di-oestrous individuals were found with cells almost as high. Any cyclicity of variation there may be is clearly much smoothed out. The nucleus of a ciliated cell does not appear ever to become seriously displaced. I find no evidence of a ciliated cell losing its cilia. These cells have well-developed Golgi bodies, and they do not show regular or obvious degeneration.

The non-ciliated cells have usually been contrasted with the ciliated cells as being secretory, but they are not in fact conspicuously active in this way in the mouse. It is these cells, however, which are concerned with the most striking and puzzling phenomenon of the oviduct: the displacement of the nuclei, so frequently remarked upon, and apparently without a parallel in any other tissue. The process appears to be this: certain non-ciliated cells, dense after osmic fixation, and staining notably with light green, acid fuchsin, and iron haematoxylin, hitherto packed between the ciliated ones and kept back by them from the lumen, tend to bulge, and thus to break the ciliated surface. This can be seen, for instance at *B* in text-fig. 2. This bulge or bubble of cytoplasm is at first clear, but tends to darken later, when certain irregularities or inclusions can be made out in it. The Golgi body of the cell may extend, by the development of a process, into the bulge.

The appearance of the epithelium when this is taking place—and it takes place constantly to a greater or less degree—is reminiscent of the condition figured by Snyder (6, 7) for the pig and human oviducts, though in the mouse the non-ciliated cells are bulging rather than the ciliated retreating. The cell which has developed this bulge has all this time remained in contact with the basement membrane. It is by now very thin and dense, and its nucleus is much compressed. The nucleus now begins to glide towards the bulging end. At the same time the inner end of the cell retreats from the basement membrane. This produces an appearance like that shown at *D* in text-figs. 1 and 2. This is the phenomenon of nuclear extrusion described by Allen (1). It will be seen that the nucleus is not really extruded from the cell at all. It is actually still inside a thin layer of cytoplasm whose extrusion preceded its own. The nucleus may be dense, but it is not commonly pycnotic.

I have never found a nucleus free in the lumen of the oviduct, nor have I found a ciliated cell free. I have, however, in several mice, found a number of non-ciliated cells, apparently of epithelial origin, free in the lumen. Since there appears to be practically no cell division in the epithelium of the oviduct it is difficult to see how any wastage of cells could be made good. For this reason it seems likely that normally the displaced cells do not become fully detached, but move back to their original positions between and below the

ciliated ones, perhaps when these have lost some of their turgor after secretion. This would suggest that the free cells described indicate perhaps a somewhat abnormal, and possibly degenerative, condition.

In the few cases of pregnancy and pseudo-pregnancy examined the ciliated cells are large, and while some displacement is to be seen, as always, among the non-ciliated ones it does not appear that this is carried even so far in the presence of the persistent corpus luteum as it is in the normal di-oestrous phase. This seems difficult to reconcile with the view that displacement depends upon the secretions of the ovary, since no significant difference can be seen between the effects of the follicular and luteal phases. The most that can be said is that during met- and di-oestrus the secretion by the ciliated cells and the displacement of the non-ciliated cells and of their nuclei seem to reach a slight maximum.

DISCUSSION

Previous authors have described the following three types of cell in the ciliated epithelium:

(1) Ciliated cells.
(2) Non-ciliated cells called secretory.
(3) Peg cells.

From what has been said it will be clear that the peg cells are really the thin dense cells found between the lighter ones, whether they are ciliated or not. The term peg cell therefore, since it has been used to cover any cell which is thin and dense at a given moment, does not seem to represent a real class of cellular element. Its usefulness then appears to decrease as the analysis of the situation is pushed further. Unless definite evidence of the change of ciliated cells into non-ciliated or of non-ciliated into ciliated can be found, it seems that the most useful distinction remaining is between these two types of cell. The terms *ciliated* and *secretory* must certainly not be contrasted with one another. The distinction has no reality.

The typical elements, and the most curious, are the non-ciliated cells, which probably form the majority of the so-called peg cells, and show the very remarkable phenomenon of nuclear displacement. The significance of this activity is most obscure. It does not seem closely like that of any other epithelial cell. Its relation to the oestrous cycle seems to be very slight. Since every detail of it can be observed in the mouse four to six days after birth it is manifestly idle to attempt to fit it into the scheme of changes shown by the uterus and vagina in response to the rhythmical stimuli of the ovary.

There remains the possibility that these events may be related to the passage of the egg, and represent the vestiges of the processes leading to the great tertiary accretions in some forms. It has not so far proved possible to demonstrate any homology of this kind. The theory that the elements showing displacement are leucocytes receives no support from this investigation; they appear always to be outside the basement membrane.

CONCLUSION

While the outer portion of the Müllerian duct gives rise to the uterus and vagina lined with epithelia whose behaviour is intimately affected by the march of events in the ovary, the inner portion produces epithelia one of which exhibits, in the displacement of cells and nuclei, a behaviour which is apparently unique, but which yet cannot be closely related to any cycle.

I wish to express my very great gratitude to Prof. F. W. R. Brambell for advising me at the beginning of the work and during its progress, and for reading the paper in typescript and for making many invaluable suggestions. My thanks are also due to Prof. A. C. Hardy, in whose Department the work was done, for his unfailing kindness and encouragement, and to Miss M. L. Paton who is responsible for the drawings.

POSTSCRIPT

Since the conclusion of this work a note has been published by Burrows (8) describing some effects of oestrin upon the derivatives of all levels of the Müllerian system in the male. The present indications are (Burrows, private communication) that a gradient in reactivity to oestrin is present in the Müllerian vestiges in the male, descending from the exterior, that is to say from the opening of the ducts into the prostatic urethra towards the periphery of the prostate and coagulating glands, comparable with that described in the female, where the vagina is affected in the normal cycle most and the oviducts least.

This suggests that there is, in addition to a remarkable tissue-specificity of reaction, some fundamental spatial susceptibility-gradient in the system. The real nature of this gradient might repay elucidation.

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EXPLANATION OF PLATE I

Fig. 1. Section through internal genitalia of adult female mouse. ×45.
Fig. 2. Epithelium lining the isthmus of an adult female mouse. ×600.
Fig. 3. Epithelium lining the ampulla of an adult female mouse at late oestrus. ×530.

EXPLANATION OF LETTERING

Am. Ampulla.
B. Bulging cell.
D. Displaced nucleus.
F. Fimbriated funnel.
Ist. Isthmus.
Ut. Uterus.

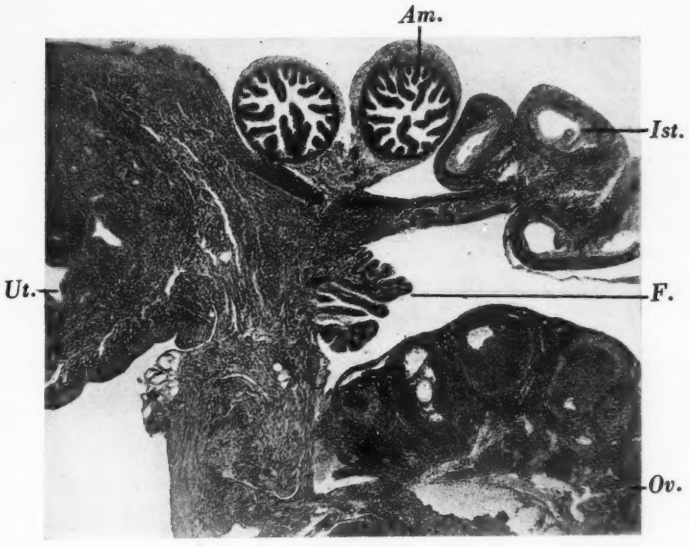

Fig. 1.

Fig. 2.

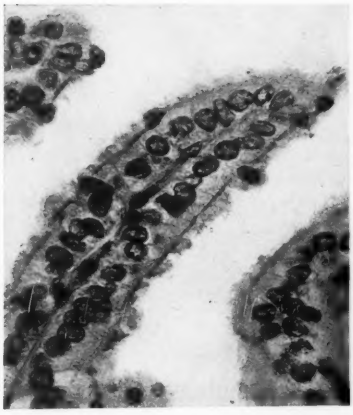

Fig. 3.

THE DEVELOPMENT OF NERVE ENDINGS IN THE HUMAN FOETUS

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University Reader in Histology at the London (Royal Free Hospital) School of Medicine for Women

The development of nerve endings in the various tissues of the body is so closely bound up with the histogenesis of those tissues that any investigation of the former must include the latter, more particularly as the developing nervous elements are known to be influenced by their surroundings. Thus Detwiler (1) showed the attraction exerted by the limb buds for the growing motor nerves: Tello (2) speaks of the neurotropic attraction of developing muscle fibres for sensory nerves, and within the nervous system itself the directional growth of nerve fibres and final position of nerve cell groups appears to be determined largely by metabolic activity both local and peripheral, the process being known as neurobiotaxis (Kappers (3)).

The histogenesis of motor and sensory nerve endings in the chick has been described in great detail by Tello (2), who, in addition, gives an account of the differentiation of striped muscle cells: this account includes some few references to nerve endings in the human foetus of 6 months and at full term. Langworthy (4) refers to the presence of spindles in practically all muscles from the fourth month, although they were not demonstrated in the diaphragm nor in most of the intrinsic tongue muscles. The development of the muscles and their nerve fibres in the human foetus is referred to by Frazer (5), who states that during the fifth week muscles are indicated in the form of pre-muscle masses in the mesenchyme, and that at or before the 10 mm. stage the main nerves of the limbs are found within it: he says, further, that by the middle of the second month the sympathetic fibres have reached all the important rudimentary organs of the trunk, and that taste buds appear during the third month.

Other references to the *development* of the nerve endings in the human foetus are very scanty, although the fully differentiated endings are fully described in the current text-books (e.g. Maximow (6)). Recently Boeke (7, 8, 9) has described autonomic nervous networks and endings in connective tissue and various organs in Man.

CLASSIFICATION OF TYPES OF NERVE ENDINGS

Nerve endings are perhaps best considered in relation to the organs innervated. The following summary includes the more important (6).

A. *In muscle and tendon*

(1) *Striated muscle.*

(*a*) Motor. Hypolemmal. End-plates.

(*b*) Sensory.

(i) In muscle

(α) Interstitial.

Simple branchings in connective tissue between muscle fibres.

Encapsulated Golgi bodies.

(β) Epilemmal.

Simple nerve net enveloping muscle fibres.

Complex spindles.

(ii) In tendon

(α) Interstitial.

Simple branchings.

Encapsulated Golgi bodies and Pacinian corpuscles.

(β) Epitenal.

Complex Golgi organs.

(*c*) Sympathetic. Rich plexus in relation with the blood vessels, and in the interstitial connective tissue (7).

(2) *Smooth muscle.*

(*a*) Network with branching fibres ending in bead-like thickenings possibly within the cells.

(*b*) Various sensory endings in connective tissue between muscle bundles.

(3) *Cardiac muscle.*

Probably similar to smooth muscle.

B. *In epithelial tissue*

(1) *In glands.*

Network outside the basement membrane with branches that make a second network on the inner surface: thin, branching varicose threads ending with thickenings between the cells.

(2) *In epithelial layers.*

Several superimposed networks, with varicose threads ending between the cells. Also special tactile cells.

C. *In connective tissue*

(1) *Free endings.*

(*a*) Nerve nets.

(*b*) Arborised terminal branchings.

(*c*) Non-encapsulated glomeruli.

(2) *Encapsulated endings.*

(*a*) Encapsulated glomeruli.

(*b*) Meissner's tactile corpuscles.

(*c*) Krause's end bulbs, and Pacinian corpuscles.

(3) (?) *Sympathetic plexus.*

Throughout all tissues of the body (7).

In the present investigation only a few of these various endings have been identified, namely: in striped muscle motor end-plates, interstitial Golgi bodies, epilemmal spindles; in smooth muscle and cardiac muscle the branching network with varicose fibres; in epithelial tissue the branching fibres from the network with their varicosities in both glands and epithelial coverings; and in connective tissue the free endings and Pacinian corpuscles and the (?) sympathetic plexus. In all probability the other kinds of endings can also be found in their various stages of development, and as suitable material comes to hand it is hoped to extend the present rather fragmentary observations.

The minute structure of the various types of fully formed nerve endings has been described in detail for various animals and in some cases for the human (see Maximow (6), Tello (2)): the present investigation confirms these descriptions for the human nerve endings and traces out their development.

PRESENT INVESTIGATION

A. Material and methods

The material used in this investigation consists of human foetuses of the following approximate ages:

*6 weeks (16 mm.)	1 specimen	12 (or 12+) weeks	4 specimens
7 weeks	1 specimen	14 weeks	1 specimen
*7½ weeks (25 mm.)	1 specimen	20 weeks	1 specimen
8 weeks	1 specimen	22 weeks	1 specimen
*8+ weeks	1 specimen	26–28 weeks	2 specimens
10 weeks	2 specimens	F.T.	2 specimens

Only material showing no post-mortem changes has been used; this is difficult to obtain, accounting for the gaps in the series. Most of the specimens were fixed in 7 per cent. formalin, and then treated by a silver-pyridine method (10). Serial sections, cut at 8 or 10 μ, were mounted in Gurr's neutral mounting medium. It is important to have serial sections when looking for nerve endings as most misleading appearances can be produced by oblique sections of nerve trunks when these are altering their plane of direction. The three specimens marked * were fixed in formalin as usual, imbedded, cut serially at 10 μ, and stained with Scott's haematoxylin and Biebrich scarlet or with Mallory's aniline blue connective tissue stain: these showed the muscle and nerve trunks but not the nerve endings. In addition, muscle from many of the specimens was fixed in formalin or formo-acetic Müller, and the sections stained with haematoxylin and Biebrich scarlet, with Mallory's connective

tissue stain, and with Weigert's resorcin-fuchsin stain. The ear of one specimen was treated by de Castro's (11) method.

B. Results

The results obtained are most conveniently considered under the following headings:

(1) Differentiation of striped muscle and tendon, and of their sensory and motor nerve endings.

(2) Differentiation of nerve endings in

(*a*) Smooth muscle.

(*b*) Cardiac muscle.

(*c*) Epithelial tissue.

(*d*) Connective tissue.

(1) *Differentiation of striped muscle and tendon, and of their nerve endings*

6 ***weeks*** **(16 mm.).** The muscle cells are not yet differentiated.

7 ***weeks.*** At this age the muscle masses of the limbs consist of fusiform cells elongated for the most part in the longitudinal direction of the future muscle: these are the myoblasts of Tello in which no fibrils can be seen. The extrinsic eye muscles are only just beginning to differentiate, but in the tongue there are already fine muscle fibres with peripheral fibrils showing very fine cross-striations and several central nuclei: these are Tello's myocells. No nerve fibres were seen in the distal parts of the limbs. In the tongue, however, there is already a rich supply of nerve fibres, many with terminal swellings, particularly in relation to the finely striated developing muscle fibres.

7½ ***weeks*** **(25 mm.).** The limb muscle cells still possess neither fibrils nor striations, but many of the elongated cells contain several nuclei in a row.

8 ***weeks.*** The limb muscles are now beginning to possess fine muscle fibres showing fibrils and cross-striations, these being particularly well seen in the muscles of the hand and of the foot and in the sole. The number of nuclei within the cells is very marked; in addition the connective tissue nuclei between the muscle cells are increasing in number.

The nerve fibres in these muscles have branching and bulbous endings associated with nuclei, and lying in between and on the surface of the fine muscle fibres. It is common to see a bifurcation at the tip of the growing nerve fibre with a nucleus lying in the cleft. In addition, a very fine plexus of fibres can be made out between some of the muscle fibres: this is probably nervous and belongs to the connective tissue; it is apparently not derived from the clearly defined nerve fibre groups that are supplying the muscles (see below).

8½ ***weeks.*** Some of the muscle fibres have begun to grow considerably in girth.

10 ***weeks.*** At this stage there appears to be a very active evolution of the muscle fibres. The connective tissue between them increases very greatly,

enlarging the bulk of the whole muscle: at the same time the muscle fibres grow greatly in size, appearing as rather isolated, very bulky, fibres. These are the primitive myotubes, with well-marked peripheral fibrils and cross-striations, and a central row of nuclei; they are separated from one another by the proliferating connective tissue (see Plate I, fig. 1). The muscles of the fore-limb and hand are further advanced than those of the hind-limb and foot.

At the same time the tendons are differentiating by an increase of connective tissue elements, and loss of myotubes at these points: definite tendon fibres are not yet seen, but the elongated cells produce laminae.

At this stage of active growth and differentiation of the myotubes a definite neurotropism can be made out: the exploratory nerve fibres with their enlarged endings are related to the large muscle cells. In addition, the junctions between muscle and tendon are comparatively richly supplied with nerve fibres.

12 *weeks and* 12+ *weeks.* The very large muscle fibres are no longer apparent as the primitive myotubes are dividing longitudinally: these are now seen in groups which are separated from one another by the connective tissue, the arrangement being seen best in transverse sections. At this stage the appearance is that of very great capillary development and proliferative activity on the part of the connective tissue in addition to the multiplication of the myotubes. In those regions where development is most advanced (as in the tongue muscle) the individual fibres are becoming separated from one another by the insinuation of the connective tissue between them. At the same time the tendinous fibres are becoming differentiated with cells in rows between them.

No definite nerve endings can be made out, but the exploring fibres with knob-like terminals are very numerous, and extend to the extremities of the fingers and toes.

20 *weeks.* The division of the myotubes is now probably completed: the muscle fibres are slender, and possess well-marked fibrils and striations, but the nuclei are still central.

At this stage comparatively complex sensory nerve endings are present in the muscles of the arm and the leg both of the epilemmal spindle type and of the interstitial Golgi body type (see Plate I, fig. 2). None were seen in the tongue muscles which are more fully differentiated than those of the limbs, but on the other hand there is in the tongue a beginning of differentiation of rudimentary motor endings associated with nuclei on the surface of the muscle fibres.

22 *weeks.* The nuclei in some of the muscle fibres are now in a peripheral position, due either to an active migration or to an increase in fibril material.

The developing sensory organs are very numerous in the muscles of the hand, and rather less numerous in those of the foot.

26–28 *weeks.* The muscle fibres, although still slender, present a finished appearance; the nuclei are now peripheral and the whole fibre is filled with fibrils; the cross-striations in the fibrils look typical. The connective tissue

between the fibres is not so marked. From this stage onwards the muscle fibres increase in length and in girth, without showing any real modification of structure. The nerves of the tongue muscles now show complex but unfinished motor plates, the terminal branchings and swellings being well differentiated and associated with numerous nuclei (see Plate II, fig. 1). The sensory endings of the limb muscles still have terminal knobs and are not yet completed. The motor endings in the forearm muscles are just beginning to differentiate.

Full term. The sarcolemma of the various muscle fibres does not seem to be complete until the motor end-plates are differentiated. It is very noticeable that all the muscles do not differentiate at the same rate, the tongue muscles being among the earliest and apparently completed in detail at birth: the extrinsic eye muscles are among the latest to differentiate, and at all stages the muscles of the foot and of the leg lag behind those of the hand and of the arm.

At birth the sensory nerve endings have a "finished" appearance, but the motor endings of the limb muscles, particularly of the foot and of the leg, are not yet nearly completed. The motor plates in the tongue, the intercostal muscles and the diaphragm are, on the other hand, highly differentiated at full term.

(2) *Differentiation of nerve endings*

(*a*) *In smooth muscle.*

10 *weeks.* The smooth muscle of the gut and of the bronchioles possesses numbers of isolated nerve fibres, but no endings were seen. The smaller blood vessels and capillaries already possess a rich plexus, which may be part of the connective tissue plexus (see below).

14 *weeks.* Auerbach's plexus is well developed although fine: Meissner's plexus is also present.

26–28 *weeks.* The media of larger blood vessels is innervated: probably these fibres have also been present in the younger specimens.

(*b*) *In cardiac muscle.*

10 *weeks.* The heart is richly innervated, particularly in the neighbourhood of the sino-auricular node: a plexus is present and fibres can be made out in the auricular walls, and in the interauricular septum; only very few fibres are present in the ventricles. At this stage the nerve endings appear varicose. It is not possible in these preparations to say whether the fibres are of sympathetic or of parasympathetic origin.

(*c*) *In epithelial tissue.*

7 *weeks.* There is a rich nerve supply just beneath the epithelium of the tongue.

8 *weeks.* The skin of the toes is supplied by a network immediately below the epithelial cells.

10 *weeks*. The lung alveoli and bronchiole epithelium is innervated by fine branching fibres just below the lining cells. The mucous membrane of the tongue has a rich network just below the surface epithelium. Free nerve endings are present between the specialised sensory epithelial cells of the cochlea and of the maculae of the inner ear.

12 *weeks*. The plexus beneath the skin epithelium is very complex, and is particularly well marked below the surface in the penis.

20 *weeks*. Free nerve fibres can be seen ending in the Malpighian layer of the skin. The tongue papillae are richly innervated, and although no definite taste buds were seen free nerve endings can be seen among the epithelial cells. The subepithelial plexus is very marked. The lingual glands possess nerve fibres, but apparently no nervous network nor terminations.

22 *weeks*. The developing sweat glands are innervated, but have no characteristic nervous plexus nor endings.

26–28 *weeks*. Free nerve endings are numerous among the epidermal cells, the dermis possessing a rich subepithelial plexus. The lingual glands now have a plexus innervation, while in the sweat glands this can hardly be made out.

Full time. The sweat glands are not yet fully developed, but a simple nervous plexus can sometimes be made out just outside the secretory cells.

(*d*) *Connective tissue.*

(i) *Free nerve endings*. Plexuses which are probably nervous (see below) are of very early appearance and widespread distribution: they are possibly autonomic in origin.

7 *weeks*. The corium of the tongue already possesses a plexus.

8 *weeks*. A primitive-looking plexus is present in the connective tissue between the developing muscle fibres of the limbs. Very few nerve fibres seem to be passing towards developing bone and cartilage.

10 *weeks*. The plexus between developing striped muscle fibres is very rich and fine (see Plate II, fig. 2): a similar plexus is present in the connective tissue in relation to the capillaries. Many of these plexus fibres appear to be related to cells with long processes that look like embryonic ganglion cells (see below).

12 *weeks*. The great capillary development of this stage is associated with an increasing complexity of the plexuses related to both the capillaries and the larger blood vessels: the fibres of the network possess varicosities, and some show terminal swellings. The plexus in the connective tissue of the muscles is interwoven with the muscle fibres, apparently lying entirely outside them.

At this stage also the sympathoblasts of the ganglia in the sympathetic chain show the rosette arrangement (12) so characteristic of their functional grouping and migration.

Full time. The plexuses of the connective tissue are well marked between the muscle fibres, and in fact in almost all places where connective tissue is

found. The network is now finer, more spread out, and associated with fewer nuclei than before (see Plate III, fig. 1).

(ii) *Encapsulated nerve endings.* **20** *weeks.* Developing Pacinian corpuscles were first seen at this stage in the sole of the foot: they are of a relatively simple type.

26–28 *weeks.* Comparatively complex Pacinian corpuscles are present in large numbers among the muscle masses of the thumb.

Full time. Although still small, the Pacinian corpuscles in both hand and foot look very "finished" (see Plate III, fig. 2).

DISCUSSION

The histogenesis of striped muscle in the human takes place in the same way as that of the chick, which has been so fully described and illustrated by Tello (2). This worker has also followed out in great detail the differentiation of the main types of sensory and motor nerve endings in the chick, and the present investigation shows that in the human the order of their development and the different stages of differentiation are quite comparable. As, however, the whole period of development up to hatching in the chick is only 21 days, whereas in the human it is about 40 weeks, the variations in individual muscles and organs is much more readily seen in the latter. The accompanying table shows a comparison between the stages in the chick and in the human of histogenesis of striped muscle and of some sensory and motor nerve endings.

Striped muscle and tendon	Sensory nerve endings	Motor nerve endings	Human (approximate age) weeks	Chick (Tello) (approximate age) days
Beginning differentiation	—	—	7	5
Myofibrils appear	Exploratory fibres with bulbous endings penetrate into muscles		8	6
Great increase of connective tissue. Vast numbers of nuclei	—	—	—	6–7
Isolated "fat" fibres	—	—	10–12	7
	Varicose endings in contact with myotubes	—	10	—
Tendon fibres differentiate	—	—	12	10
	Beginning Pacinian bodies	—	20	11
Multiplication of myotubes	—	—	12–22	9–13
	Spindles differentiate	—	20	12
Dissociation of myotubes from one another. Nuclei become peripheral	Spindles become complex	—	22–26	13
	Pacinian bodies well developed	—	26–28	15
		Plates begin to differentiate	26–28 (very rudimentary except tongue)	18

Several points of interest emerge from a consideration of the relative times of development of the nerve endings. Perhaps the most striking fact, to which others have already drawn attention, is that the evolution of the sensory nerve endings is more or less completed before that of the motor endings has begun. In the human the motor plates begin to differentiate at about 26–28 weeks, but at first these are very rudimentary except in the tongue muscles: these muscles, which are among the first to differentiate, look more nearly completed than do those of the limbs at this age. Tello has suggested that there is a relationship between the formation of the motor endings and the functional activity of the muscle, and this is supported by the finding that at an age when the foetus is viable the tongue muscles possess complex motor endings while the limb muscles do not, and even at birth the motor endings in the diaphragm and intercostal muscles are considerably further developed than are those of the limbs.

The sensory endings in the tongue muscles cannot be very numerous: none were identified in this series, although they must be present.

The differentiation of the muscles and of the sensory innervation is further advanced in the hand and arm than it is in the foot and leg at all stages of development, the difference being noticeable even at 10 weeks and persisting until birth.

The innervation of the lingual glands and of the sweat glands is of interest. The nerve plexus arrangement that gives rise to fine, branching, varicose fibres that penetrate among the secreting cells, was not seen in the glands of the tongue until 26–28 weeks, that is the age at which the foetus can live and suckle, and the same age at which the real motor endings of the tongue muscle fibres are developing. Mucin-secreting cells are differentiated about this time also in the salivary glands (13). The sweat glands are not fully innervated even at birth, the external nerve plexus being still very rudimentary: this may be a contributory factor in the inability of the new-born child to regulate its own temperature, although sweat can be produced.

If the plexus of the connective tissue described here is the same as that described by Boeke (7, 8, 9) it is of very early appearance, being distinctly differentiated in the connective tissue between the developing muscle fibres by 8 weeks: the fibres are quite distinct from those supplying the future sensory and motor endings. He regards the plexus as "sympathetic" and describes it as "a syncytial arrangement of the protoplasm of the lemmoblasts with the neurofibrils imbedded in it—Lawrentjew's 'interstitial cells'": the plexiform anastomosing bands of neurofibrillae run along capillaries adhering to the endothelial wall, encircle and envelop striated muscle, make a network round clumps of gland cells and from this network spring the fine fibres which run between the gland cells: it is found in the connective tissue. It is not always easy to demonstrate this plexus, but the silver technique used in this investigation usually gives a good impregnation of an argentophil plexus. (The Fischer-Ranvier gold chloride method (14) will also frequently show up

a similar plexus.) In the younger stages the impregnated cells of the plexus are relatively more numerous than in the older stages when the plexus fibres are presumably stretched out somewhat by growth. It is possible that this plexus is not nervous at all, but the impregnation of the fibres is of the same type as that of undoubted nerve fibres, and some of the cells connected with them have long processes and look as if they must be of nervous nature. If these elements are nervous, they probably represent the sympathetic elements (15). Further investigation of this point is in progress.

SUMMARY

1. The histogenesis of striped muscle takes place in the human in the same way as in the chick.

2. The differentiation of the various voluntary muscles occurs at different stages of foetal development.

3. There is a relationship between the stages of muscle differentiation and the development of the nerve endings in the muscle.

4. Sensory nerve endings are almost completely developed before the motor endings begin to differentiate.

5. Muscles and nerve endings are differentiated first in the tongue: at all stages the neuromuscular mechanism of the hand and arm is further advanced than that of the foot and leg.

6. An argentophil fibre plexus is already present at 8 weeks' development: this may perhaps be the fundamental sympathetic plexus.

7. By 20 weeks' development Pacinian bodies and spindles are well differentiated: by 28 weeks the motor plates are just beginning but are very rudimentary except in the tongue.

8. The functional significance of the ages at which certain nerve endings develop is discussed.

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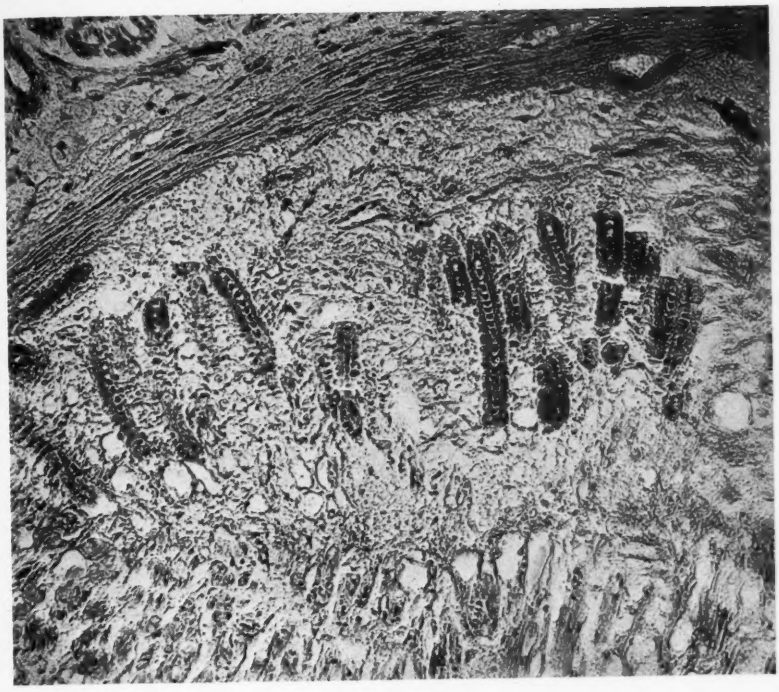

Fig. 1.

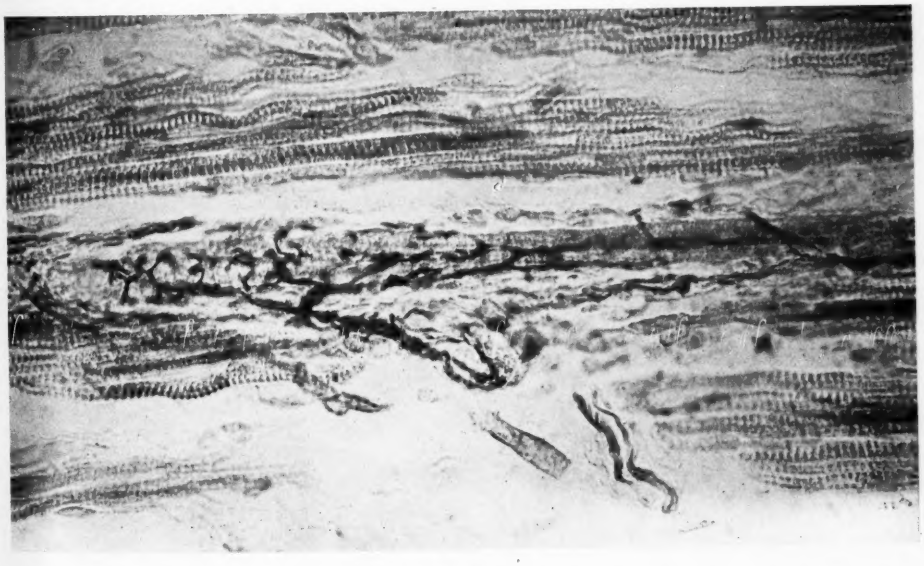

Fig. 2.

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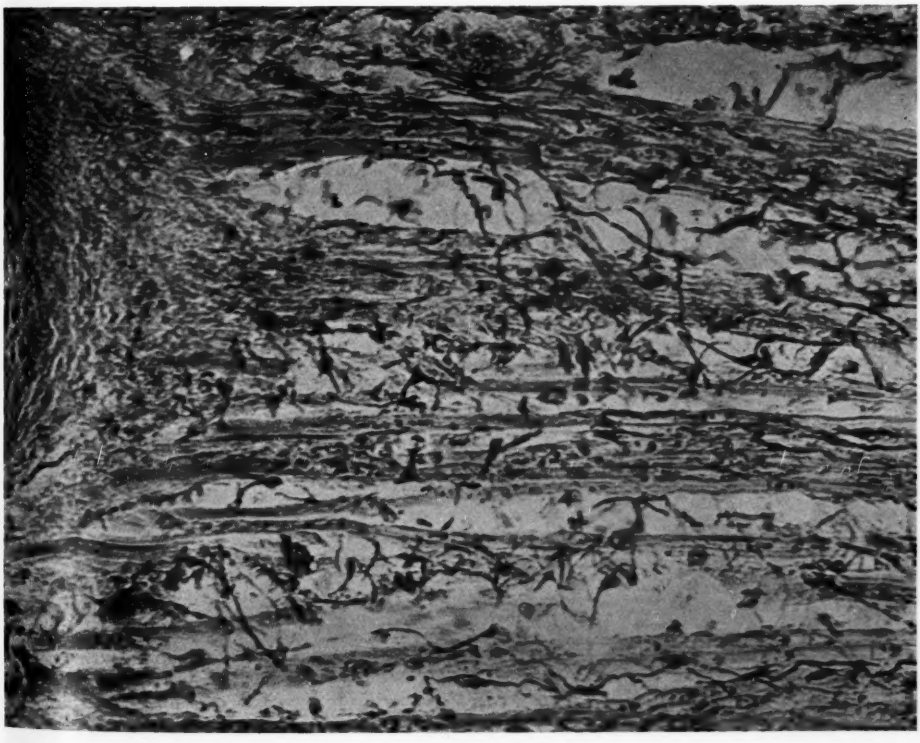
Fig. 1.



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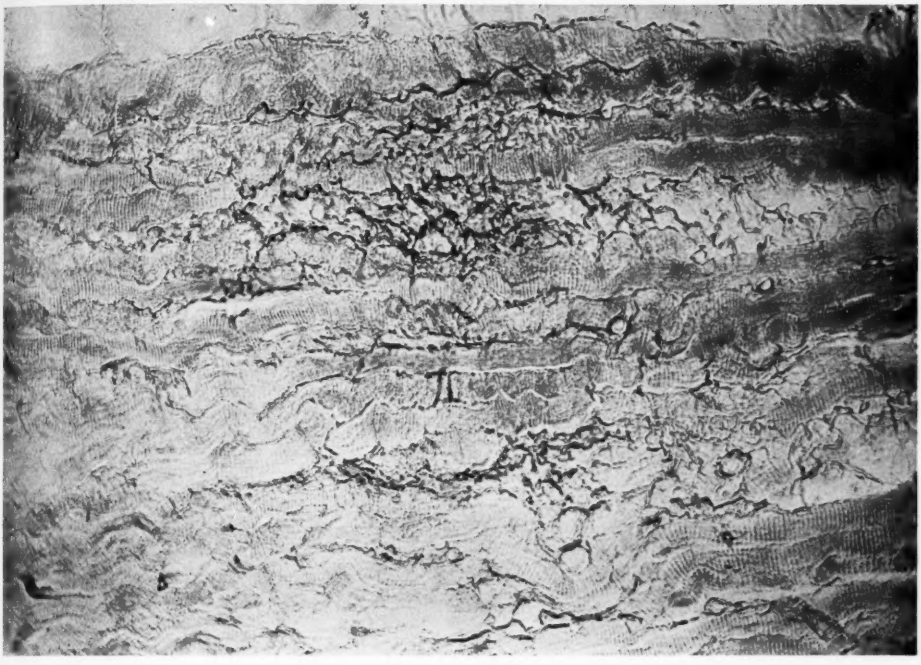

Fig. 1.

Fig. 2.

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EXPLANATION OF PLATES I–III

(Untouched photomicrographs)

Plate I

Fig. 1. Developing striped muscle fibres. Foetus of 10 weeks. (No. 21.) ×250.
Fig. 2. Developing sensory nerve ending in the muscles of the forearm. Foetus of 20 weeks. (No. 60.) ×500.

Plate II

Fig. 1. Developing motor nerve endings in the muscle of the tongue. Foetus of 26–28 weeks. (No. 6.) ×500.
Fig. 2. Argentophil plexus among developing muscle fibres of the foot. Foetus of 10 weeks. (No. 67.) ×500.

Plate III

Fig. 1. Argentophil plexus among muscle fibres of the hand. Full-time foetus. (No. 80.) ×500.
Fig. 2. Pacinian corpuscles from the sole of the foot. Full-time foetus. (No. 80.) ×300.

THE CEREBRAL HEMISPHERES OF THE KIWI AND OF THE EMU (*APTERYX* AND *DROMICEIUS*)

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Studies of the cerebral hemisphere of the kiwi reported by the present writer (1929, 1930) and by Durward (1932), despite substantial agreement, revealed certain differences of opinion which it is desirable to examine further. New material of the kiwi brain being unlikely to become available at present, and some light having been thrown upon certain points by examination of and comparison with the brain of the emu, the evidence thus obtained, in so far as it appears to be significant in relation to conditions in the kiwi, will be briefly discussed.

The material upon which the present observations are based is the same which has been described in the author's previous reports (1930, 1935), namely a single brain of *Apteryx australis* cut transversely into sections 30 μ thick, alternate sections being mounted so as to provide two series, which were stained respectively with carbol thionin and with iron haematoxylin; and two brains of the emu (*Dromiceius novaehollandiae*), one of which was cut transversely and the other sagittally, at a thickness of 40 μ, each again being mounted as two series, stained respectively with cresyl violet and with Weil's fibre stain. The *Apteryx* brain was referred to in the 1930 paper as the Sydney specimen. For all three of these specimens the author is indebted to the generosity of Dr A. N. Burkitt of the University of Sydney. A single left hemisphere of the ostrich (*Struthio molybdophanus*), presented by Dr C. U. Ariëns Kappers, sectioned transversely and prepared as in the case of the emu brains, has also been used for comparison. This material will be described in a later paper.

Attention will be directed mainly to certain features of the pallium.

HIPPOCAMPAL FORMATION

It is unnecessary to add anything to the general descriptions of the hippocampal formation of *Apteryx* given by Durward (1932) and by the present writer (1930). Regarding the dorsal boundary of the formation, however, it may be remarked that, while the deepest layer is continuous with the deeper part of the parahippocampal cortex dorsally, the boundary is distinct at most levels in the medial two-thirds to three-quarters of the wall; and the myelinated fascicles of the septomesencephalic tract do not, in the writer's sections, run

through this boundary, as Durward's description (p. 456) seem to imply, but come ventro-mediad through the more ventral part of the parahippocampal region, as in the emu (Craigie, 1935).

In the emu, the hippocampal formation was found to be divisible into four longitudinal zones, designated, ventro-dorsad, *H* 1, *H* 2, *H* 3, and *H* 4. Comparison of the description of these and of Plate I, fig. 2, with the account of the formation in *Apteryx* and with the photograph reproduced herewith (Plate I, fig. 1) will show that they are present in the latter also, and have practically the same characteristics, though they were not formerly given special designations. The region distinguished by the non-committal mark *H* 1 is that termed fascia dentata in the description of *Apteryx*.

The account of Durward gives no indication of the presence of the division *H* 2, and his drawings suggest it only in his fig. 22, but a re-examination of the present writer's sections shows that, as in the emu, there is a rather narrow region ventral to *H* 3, in which there is only one cell layer, instead of the three layers present in the latter (Plate I, fig. 1). It is by no means sharply marked off, but the cells are a little larger than in the medial part of *H* 3, with which the region is continuous. Behind the level of the foramen of Monro, *H* 2 becomes hardly recognisable, but is probably still present as a narrow oblique zone of cells overlapped by *H* 1.

In the anterior part of its extent, the hippocampal formation is nearly a uniform plate of cells. When followed back, however, the small-celled medial group distinctive of *H* 4 soon appears at its upper edge. In sections passing through the interventricular foramen, the three-cell layers of *H* 3 also become recognisable and pass over ventrally into the one-cell-layered *H* 2, which here has its greatest width. *H* 2 narrows ventrally into a thinner plate of smaller, darker cells, covered by a slightly thinner zonal layer. This is *H* 1, or the fascia dentata, which expands greatly behind the level of the foramen. Durward describes this plate as entirely post-foraminal and emphasises its sharp definition from the hippocampus dorsal to it, points which do not seem to fit precisely the conditions in the specimen available. He also emphasises its overlapping the medial band of cells of the hippocampus dorsal to it. This is suggested at the more caudal levels, where *H* 2 fades into an indefinite oblique band of cells, as indicated above, but elsewhere is not clear in the sections studied.

The whole hippocampal formation curves round the medial aspect of the occipital pole, so that, as the transverse sections are followed back, it appears in inverted position in the ventral part of the section, as described in the previous paper (1930). A little farther back the dorso-medial and the ventral parts become connected in the sections by a continuous line of formation *H* 1, which eventually fades out, to be replaced by the other subdivisions, though these become less distinct. *H* 2 is practically unrecognisable, and *H* 3 and *H* 4 change their appearance somewhat, most of the cells being much smaller than in the dorso-medial part of the formation, though the cells of the super-

ficial cell layer of *H* 4 are larger and less crowded than in its more characteristic regions.

While this general arrangement was recognised before, serious error entered into the identification and description of the parts, as became clear in the study of the emu.

The dorso-medial part of the hippocampus in the available specimen of *Apteryx* is bounded dorsally by a slight fissure, which was interpreted as hippocampal fissure. Durward found this also in his material, and called it pseudohippocampal fissure.

In the ventro-lateral part of the occipital portion of the hemisphere, appears a wide groove (1930, fig. 10), which was formerly believed to be continuous with the so-called hippocampal fissure round the occipital pole. Durward questioned the correctness of this belief, and further study has now shown it to be erroneous. The "hippocampal fissure" fades out and does not curve round the occipital pole so far as can be seen. In any case, it is not equivalent to the wide ventro-lateral furrow.

This erroneous interpretation of the fissures led to all the ventral wall of the occipital part of the hemisphere between the wide furrow and the thickening containing the "medial superposition" (1930, p. 253) being regarded as hippocampal. Actually, as made clear in the description of the emu (1935), and below, the "medial superposition" involves *H* 3 and *H* 4, and the lateral boundary of the hippocampus in the ventral wall is at the lateral edge of the "superposition", near the broadest part of the thickening (Plate I, fig. 2).

The thickening referred to extends farther forward in the ventral wall in *Apteryx* than in *Dromiceius*. On the other hand, the dorso-medial part of the hippocampal formation in the former fades out anteriorly a little in front of the level of the interventricular foramen, while in the latter it extends antero-ventrad to near the base of the olfactory bulb. This is associated with the extreme reduction of the pallial part of the medial wall anteriorly in the kiwi, where it appears only as a thin membrane, and its retention of a markedly more massive form in the emu.

The comparison of the arrangement of the cells in the longitudinal thickening with the medial superposition of Reptiles must be abandoned. The latter is considered (Kappers, 1921, etc.) to be an overlapping of the fascia dentata, or its precursor, and the hippocampus proper, and would correspond with the overlapping of these parts described for the kiwi by Durward, which, however, is not very evident in the writer's sections. The overlapping in the longitudinal thickening, on the other hand, is more probably comparable to the transition between hippocampal and parahippocampal cortex in lower Mammals (Craigie, 1930, 1935).

A rather striking correspondence between the characters and relations of the hippocampal and parahippocampal formations in the alligator and in the emu has been pointed out in the preceding paper (1935).

The septomesencephalic tract is considerably more largely developed in

the emu than in the kiwi. In the latter it does not completely fill the zonal layer of the most dorsal part of the hippocampus (*H* 4), as it does in the former (1935, fig. 7).

The deep hippocampal fibre system compared by the writer (1935) to the medio-dorsal periventricular system of Huber and Crosby (1929) is also present in the kiwi, though apparently much less well developed than in the emu.

PARAHIPPOCAMPAL CORTEX

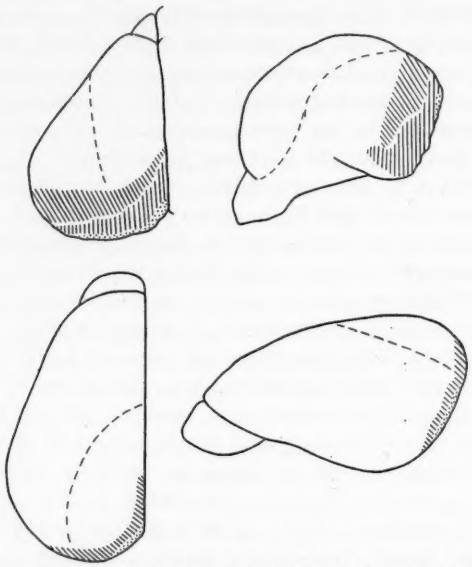
A circumscribed area with very distinct multilaminar cortex situated in the ventro-lateral part of the hemisphere of the kiwi towards its occipital end was described and figured by Craigie (1929, 1929 *a*, 1930). This cortex is believed to have been derived from part of the dorsal cortical plate of Reptiles and was consequently termed neopallial, this term being later replaced (Craigie, 1932, pp. 159 and 162) by the term parahippocampal cortex, following the usage of Elliot Smith (1919) in Reptiles. The account of this area of cortex was fully confirmed by Durward (1932), though his photograph makes it appear much less distinct than in the writer's sections.

Another portion of the "neopallial" or, better, parahippocampal cortex in the form of a narrow, somewhat wedge-shaped zone lying between the hippocampus and the hyperstriatum accessorium at the dorso-medial angle of the more caudal part of the hemisphere was also described in some detail by both Craigie and Durward. Here also there are traces of lamination, admittedly "rather irregular and somewhat indefinite; in fact, it has the appearance of a vestigial condition". The present writer, however, believed these two multilaminar areas to be continuous round the occipital end of the hemisphere, while Durward described both as fading out caudally, seeming to imply a denial of their continuity. This view was linked up with his fully justified scepticism regarding the continuity of the slight dorso-medial "hippocampal fissure" and the broad ventro-lateral furrow discussed above. Moreover, Durward considered the indications of cortical structure so indefinite that he preferred to designate the dorso-medial area simply, "medial extension of the hyperstriatum accessorium".

In the emu material, no fissure marks the dorsal margin of the hippocampal formation, and no representative of the wide ventro-lateral furrow could be recognised. A relatively wide zone of parahippocampal cortex was found to extend parallel to the hippocampal formation, however, with essentially the same relations to it as in the kiwi. It occupies all the space between the hippocampal formation and the hyperstriatum accessorium, which space is much wider than in *Apteryx*, and extends from the dorso-medial region of the hemisphere wall across the occipital end into the ventro-lateral area (text-fig. 1).

Dorso-medially, this cortex is both much wider and much more highly differentiated than in the kiwi, and where it borders the hyperstriatum accessorium, i.e. in the region where vestigial multilaminar cortex was thought by

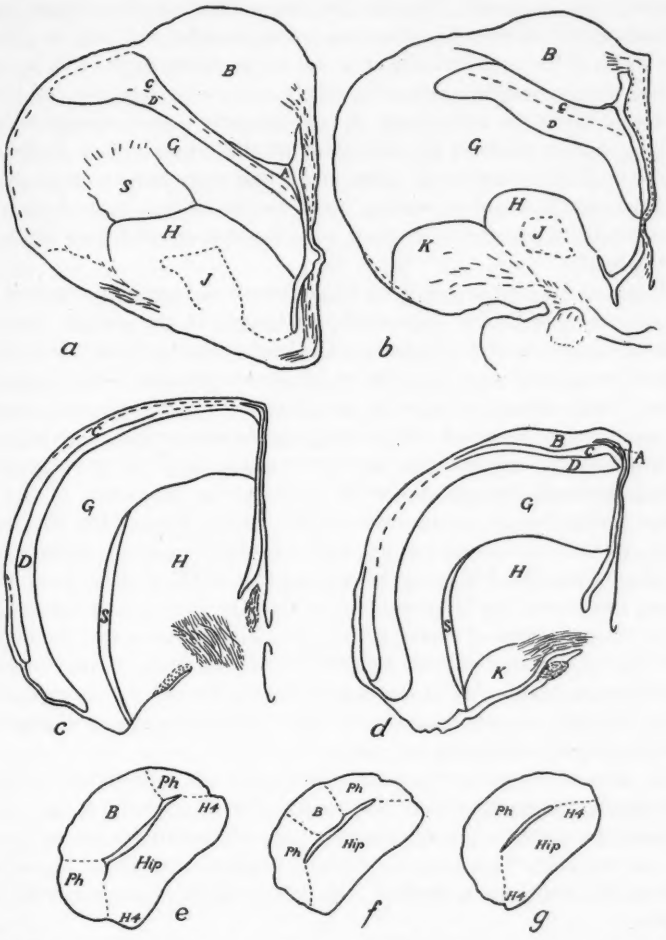
the present writer to be recognisable in the kiwi, it has a well-developed multilaminar area, which has been described in a separate note (Craigie, 1934). This area (parahippocampal subdivision *d*, Craigie, 1935) has a lamination pattern similar to that in the distinct ventro-lateral multilaminar area of the kiwi, though the more crowded layers do not have the grouping quite so close and hence are not quite so conspicuous (cf. Plate I, fig. 2, and Plate II). The multilaminar cortex extends into the region corresponding in position with the ventro-lateral area of the kiwi. A restudy of the kiwi sections leaves no



Text-fig. 1. Above, dorsal and lateral views of the left hemisphere of the emu; below, similar views of the left hemisphere of the kiwi. The area covered by multilaminar parahippocampal cortex is indicated by oblique hatching; that covered by parahippocampal cortex with only one distinct cell layer, by vertical hatching; that covered by hippocampal cortex, by stippling. The broken line indicates the lateral margin of the hyperstriatum accessorium.

doubt of the continuity of the dorso-medial and ventro-lateral areas round the occipital pole. The latter area is delimited by a slight ventricular groove from the caudal end of the hyperstriatum accessorium (text-fig. 2 *e*, *f*). The most caudal sections of the hemisphere comprise only hippocampus and parahippocampal region separated by the ventricular cleft (text-fig. 2 *g*).

In the emu, however, another broad zone of parahippocampal cortex, with only one distinct cell layer, covered by a thick lamina zonalis, separates the multilaminar area from the hippocampus. This area was found (1935) to be further differentiable into three parallel, longitudinal zones, parahippocampal subdivisions *a*, *b* and *c* (Plate I, fig. 2).



Text-fig. 2. *a*, *b*, transverse sections through the cerebral hemisphere of the emu, outlined with the projection microscope; *c*, *d*, *e*, *f*, *g*, transverse sections of the hemisphere of the kiwi. *c*, *d*, *e* are the same as fig. 6 *d*, *e* and *j*, respectively, of the 1930 paper.[1] Mag. $\times 3\frac{1}{2}$. Comparison of *c* and *d* with *a* and *b* shows how the neostriatum is extended ventrad over the lateral aspect of the hemisphere in the kiwi. *e*, *f* and *g* show the continuity of the parahippocampal formation round the caudal end of the hyperstriatum accessorium. *B*, hyperstriatum accessorium; *C*, *D*, neostriatum superius; *G*, neostriatum inferius; *H*, mesostriatum; *J*, palaeostriatum; *K*, archistriatum.

[1] It may be noted that the magnification given in the legend of fig. 6 of the 1930 paper is a misprint. It should be $\times 3\frac{1}{2}$, as here.

The dorso-medial parahippocampal cortex of the kiwi gives the impression of having been squeezed between the hyperstriatum accessorium and the hippocampal formation, this squeezing having resulted not only in a decrease in the width of the multilaminar area and in the distinctness of its layers, but also in a nearly complete reduction of the zone with only one cell layer, so that it can hardly be recognised. A few obliquely placed, elongated, deeply stained pyramids close to the boundary of the hippocampus, however, are suggestive of division *a* in the emu, and *b* and *c* are almost certainly represented where the band of cortex turns ventro-laterad, just dorsal to the hippocampus, to become continuous with the deeper cell layers of the latter (Plate I, fig. 1).

Close to the occipital pole, both hippocampal and parahippocampal formations appear considerably thickened (due largely to the oblique direction in which the transverse section here cuts the hemisphere wall) and the lamination in the latter is quite indistinct. Between the ventral edge of the hippocampus and the ventro-lateral, indistinctly multilaminar cortex, appears a small area with numerous rather small cells lacking any obvious arrangement but covered with a zonal layer broader than that of the adjacent part of the hippocampus. Working forward through the serial sections, the characters of the multilaminar cortex become more obvious, the ventral part of the hippocampus appears in the ventral thickening, and a broad depression appears, at first separating them, but following the ventral edge of the multilaminar area and drawing away from the hippocampus, so that the small-celled region expands into an extensive area of cortex between the hippocampus and the depression (Plate II). The groove referred to is that mentioned above, and erroneously called hippocampal fissure in the earlier description of this material. A more correct, though clumsy term would be *endoparahippocampal groove*. This groove is not represented in the emu.

The area of cortex between the groove and the longitudinal thickening, i.e. between the multilaminar cortex and the hippocampus, was formerly attributed to the latter, but actually represents parahippocampal areas *a*, *b* and *c* of the emu. This cortex, which is illustrated in Plate II, appears in fig. 10 of the 1930 paper, marked *AF*. It resembles rather markedly that of the emu.

In the emu it was observed, when areas *a*, *b* and *c* were traced forward in the ventral part of the lateral wall, that there "the cells become smaller and more crowded and largely lose their pyramidal character, and the subdivisions become less distinct but more extensive, spreading to form the ventral half of the lateral wall".

In the kiwi they are gradually stretched to form a thin plate extending across most of the ventral surface of the hemisphere, and have a general character similar to that indicated in the phrases just quoted. The region corresponding topographically with *a* shows a relatively extensive area of quite small cells. Area *b*+*c* (if both are represented) has somewhat larger

cells and there is little sign of differentiation between the parts. Laterally, the cells are elongated transversely and spread apart, as if the thin wall had been subjected to considerable tension where it curves round the endoparahippocampal groove to join the multilaminar area *d*.

The approximate superficial extent of the parahippocampal cortex has been plotted in text-fig. 1. The width of the band is, of course, greater than it appears there, as it is seen obliquely from both the points of view represented. The area with only one cell layer cannot be represented on account of its ventral location. Comparison of the diagrams in text-fig. 1 shows how the areas under consideration correspond in the kiwi and in the emu.

Under the heading "Other cortical fields" (i.e. other than the hippocampal) Durward (1932, p. 461) describes "one field of cells of remarkable constancy", stating that "no similarly placed zone is described in other forms and Craigie's figures do not indicate such a field in *Apteryx* distinct from the subjacent ones". Comparing Durward's drawings and description with the available sections, there appears to the writer to be no doubt that this field is the same as the indistinctly multilaminar one described on p. 101 and illustrated in fig. 3 of the 1929 paper and mentioned again on p. 262 of the 1930 paper, though Durward's account suggests that it is more sharply delimited in his material. Its characters are so indefinite and its significance so problematical that it has been passed over lightly in more recent discussions, particularly as a corresponding area has not so far been recognised in any other form, even in the emu.

HYPERSTRIATUM ACCESSORIUM

As explained in previous papers (1935, etc.) the hyperstriatum accessorium is regarded as a pallial structure formed, by divergent evolution, from the same region which in mammals has produced neocortex. Durward's recent observations on the sparrow (1934) are in keeping with this view. In *Apteryx*, Durward found the hyperstriatum accessorium delimited superficially by a vallecula, which is not evident in the specimen at hand. Hunter (1924) also found it not conspicuous in the Amsterdam specimen "though there is an ill-defined bulging on the postero-medial part of the dorsal surface of this hemisphere".

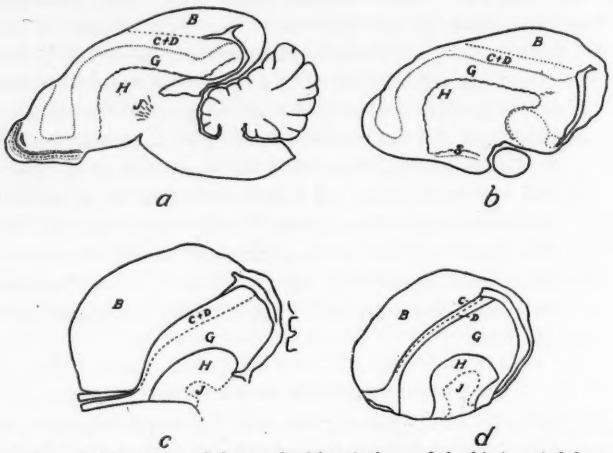
Durward, moreover, described three longitudinal subdivisions and a thin corticoid layer over the surface. These can be confirmed, though they are very indefinite in this specimen. Once more, however, it must be emphasised, as has been done repeatedly and confirmed by Durward himself, that both medially and laterally the whole thickness of the hyperstriatum accessorium tapers into the adjacent cortical or corticoid areas; so that the superficial "corticoid" layer cannot correspond with the whole thickness of the cortex, but only with an outer cell lamina. The longitudinal zones are present also in the emu.

In the former account (1930), the writer described a "caput hyperstriati

accessorii" forming a thickened cap over the anterior end of the neostriatum and passing over ventrally into the neostriatum inferius without any detectable boundary. Dorsally, a thin superficial layer of cells was considered to connect the "caput" with the "pars posterior" or main portion of the hyperstriatum accessorium.

Durward has shown that this account is incorrect, the "caput hyperstriati accessorii" being a part of the neostriatum inferius, while the "pars posterior" is really the whole of the hyperstriatum accessorium.

The hyperstriatum accessorium is thus a relatively small structure, in marked contrast to the huge mass which it forms in the emu.



Text-fig. 3. *a*, *b*, sagittal sections of the cerebral hemisphere of the kiwi copied from Durward's (1932) figs. 26 and 29; *c*, sagittal section of the right hemisphere of an emu about 2½ mm. from the median plane; *d*, sagittal section of the left hemisphere of the emu about 4·2 mm. from the median plane. Lettering as in text-fig. 2.

A peculiar feature, moreover, is its dorsocaudal position, so markedly different from its location in the cephalic and cephalo-dorsal part of the hemisphere in the emu, in the cassowary, in the ostrich (where it is even more marked), and also in the rhea.

PERIAMYGDALAR CORTEX

In this (described as "pyriform cortex"), the writer in 1930 distinguished a zonal layer with scattered cells, a dense lamina of rather deeply stained cells, and a narrow and rather indefinite layer of paler multiform cells. Durward speaks of "a fairly well localised corticoid field overlying the ventral part of the archistriatum and the adjacent part of the neostriatum from both of which it is clearly separated by a cell-free zone", and says that he cannot detect the lamination described by the writer. In the specimen available there is no clear cell-free zone under the cortex, and it would appear that this must

correspond with what was referred to as a narrow and rather indefinite layer of paler multiform cells.

A small, relatively wide, shallow groove bounding the area laterally was regarded as probably a representative of the rhinal fissure. Durward, however, found no trace of this in his three well-fixed specimens, so it may be an artefact or an individual peculiarity in the one examined. It may be noted, however, that it occurs symmetrically in the two hemispheres of that specimen.[1]

DISCUSSION

Parker (1891) pointed out that the cerebral hemispheres of the kiwi extend back over the more posterior parts of the brain to an unusual degree, completely concealing the optic lobes from above, a feature which he considered to resemble conditions in the passerine birds. This backward growth of the hemispheres he found to have, apparently, pulled with it the dorsal part of the diencephalon, resulting in a dislocation of the parts of the telencephalon medium, the diencephalon, and the mid-brain which has been described in some detail in the 1930 paper of the present writer (especially pp. 233 and 293–4). Parker's studies suggest that these changes, at least so far as the gross features are concerned, occur during ontogenetic development.

A point which was not realised fully at the time of the earlier study is that such a dislocation seems to have occurred also within the hemisphere itself; though alterations in the courses of the tracts entering into the formation of the lateral fore-brain bundle, produced by the backward extension of the hemisphere, were described (1930, p. 278). The details described in the present communication do not only correct the misapprehensions embodied in the former account. They show, further, that the hemispheres, instead of merely expanding backward and perhaps dragging and pushing the parts below and behind them, have been modified as if a shearing force had been applied to their own dorsal parts, both pulling backwards and pressing downwards.

A comparison of the accompanying outlines of sagittal sections of the kiwi and the emu (text-fig. 3) and of the diagrams in text-fig. 1 shows that the relations are as if such a force had dragged the hyperstriatum accessorium from its cephalic position to a dorso-caudal one, pulling upon the subjacent parts so that the anterior end of the neostriatum inferius is brought up over that of the neostriatum superius which seems to have remained relatively fixed. It is true that Durward considers rather that the anterior end of the neostriatum superius has grown down into the neostriatum inferius. Also, the caudal situation of the hyperstriatum accessorium in some carinatae, as noted below, lessens the value of these considerations.

This distortion might be imagined to have produced a pressure upon the pallial parts ventromedial and caudal to the hyperstriatum accessorium re-

[1] The same statements, pro and con, may be made regarding the small "amygdaloid fissure" described by the writer in 1930 but not found by Durward. At the same time, it may be mentioned that Durward's pars ventralis archistriati has not been distinguished in the present sections.

sulting in a reduction of the more anterior portions thereof, and at the same time to have influenced the reduction of the anterior part of the medial wall to an extremely thin membrane, such as occurs otherwise only in specialised avian brains like that of the parrot family. The thinness of the anterior part of the medial wall in the kiwi, as compared with that in the emu or in the ostrich, is very marked. The hippocampus cannot, as in the emu, be traced forward to near the base of the olfactory bulb. The multilaminar parahippocampal cortex is reduced to an almost vestigial condition and the parahippocampal region corresponding with areas *a*, *b* and *c* is hardly recognisable in the dorso-medial wall of the hemisphere. This region is, however, well developed in the caudal part, which has been pushed from the dorso-caudal wall of the hemisphere down on to its occipital and ventro-lateral aspects. The imagined pressure must, moreover, have squeezed the underlying striatum as well as dragging the more superficial parts. The caudal portions of the neostriatum are markedly thinned and depressed (text-fig. 3), and these areas are, furthermore, pushed down over the lateral surface of the hemisphere as well as pressed caudad (compare text-figs. 2 *a*, *b* with 2 *c*, *d*).

Thus the peculiar features of the anatomy of the hemisphere discussed in the foregoing pages have all been linked up with the strange distortion of the brain of the kiwi which was already observed by Parker. They are associated with the unusual shape of the hemisphere of this bird, which is shown not to be primitive (cf. 1930, p. 226) but aberrant.

The backward extension of the occipital poles is not comparable, as Parker suggested, with that in passerine birds, which have the hyperstriatum accessorium in a cephalic position.

Differences in the situation of the hyperstriatum accessorium, or of the corresponding eminence on the gross hemisphere, have been pointed out by numerous observers. Bumm (1883) found that a study of the brains of a representative series of carinate birds enabled him to divide them into two groups, namely, the pigeons, the predaceous birds, and the gallinaceous birds, in which the hyperstriatum accessorium (*Wulst*) reaches the anterior end, but not the posterior end of the hemisphere; and the swimming, wading, and clambering birds, in which it extends to the caudal end of the hemisphere, or nearly so, leaving the cephalic pole uncovered. Turner (1891) noted the varying positions of the vallecula in carinate birds, and found all intermediate stages between the extremes. Rose (1914) stated that the hyperstriatum accessorium (his field *B*) always reaches the frontal pole except in the Psittacidae. Küenzi (1918) assembled birds into three groups on the basis of the relations of the vallecula. Dennler (1922) distinguished thirteen types of *Sagittalwulst*, of which three, the *Anatidentype*, the *Picidentype*, and the *Psittacedentype*, reach the occipital pole. The *Struthionidentype*, corresponding with the condition in the emu described above, he states to occur in Struthionidae, Rheidae, Dromaeidae, and Casuariidae. Dennler, further, concluded that closely related avian families have the same type of *Wulst*, while simi-

larity may also appear between families which are not closely related, as a result of convergence.

If Dennler's conclusion is applicable to the ratite birds, the isolated position of *Apteryx* as opposed to the other families of the group, which agree in this feature of cerebral anatomy, is very striking. While an extensive comparative series of avian brains, such as would be required to check the facts, has not been available, the author has not noted any account of another form with caudally situated hyperstriatum accessorium showing distortions of the neighbouring parts similar to those associated with that feature in the kiwi, which would thus appear possibly to be uniquely modified.

What agent or agents may have been responsible for the production of these characters it is not possible at present even to suggest. The thought of correlation with feeding habits calls for comparison with the brain of the woodcock, in which these habits are somewhat similar. The external form of this brain was described and illustrated by Herrick (1893). It also is much modified in shape, but not in a way comparable to conditions in the kiwi, being extremely flexed. The hyperstriatum accessorium, however, is caudodorsal in position, and apparently fairly large. Further points of interest for the comparison cannot be learned from Herrick's brief description.

SUMMARY

A restudy of the sections of a brain of the kiwi previously described and comparison with two emu brains has led to the following conclusions:

1. The hippocampal cortex is structurally similar in the two forms, and may be divided into four longitudinal zones.

2. Of these zones the two middle ones (*H* 2 and *H* 3) are not very distinct from each other. The most dorsal (*H* 4—probably corresponding with area *Y* of Rose (1914)) is continuous both with *H* 3 and with the deeper layers of the cortex dorsal to it, but is quite distinct.

3. The hippocampal formation in the emu can be traced forward in the medial wall to near the base of the olfactory bulb, but does not extend nearly so far forward in the kiwi, where the anterior part of the medial wall is reduced to a very thin membrane.

4. Caudally, the hippocampal formation curves round in the medial part of the occipital wall of the hemisphere and extends forward a short distance in a thickening in the ventral wall. It does not, however, include so much of the ventral wall as was attributed to it in the earlier description by the present writer, which was erroneous also in comparing the region of the longitudinal thickening with the reptilian medial superposition. This thickening is comparable rather with the transition between archi- and neocortex in Mammals.

5. In the emu, a broad zone of parahippocampal cortex lies directly dorsal to the hippocampus and is divisible into a multilaminar portion, which is most dorsally situated, and three less distinctly differentiated bands with only one cell layer.

In the kiwi the multilaminar cortex is present in a reduced condition dorso-medially and is continuous round the occipital pole with a ventro-lateral area where it is even better developed than in the emu.

6. The parahippocampal cortex with only one layer of cells, on the other hand, can hardly be recognised in the dorso-medial region but is well developed in the caudal part of the ventral wall. It is there separated from the multilaminar portion by a broad endoparahippocampal groove which was wrongly called hippocampal fissure in the former description.

7. Both hippocampal and parahippocampal formations occupy a less dorsal position in the occipital wall in *Apteryx* than in *Dromiceius*.

8. The hyperstriatum accessorium is much smaller in the kiwi than in the emu (or cassowary, ostrich or rhea), and is situated in a caudo-dorsal position instead of in a cephalic location, as in all other ratite birds.

9. The caudal location of the hyperstriatum accessorium, the curving up of the neostriatum inferius round the anterior end of the neostriatum superius, the reduction of the dorso-medial parahippocampal cortex, the relatively ventral position of the parahippocampal cortex in the occipital wall, and possibly the extreme thinness of the anterior part of the medial wall, with the corresponding total absence of hippocampus therefrom, may all be correlated with the distortion previously observed more particularly in the diencephalon and the telencephalon medium but also involving the hemispheres. This distortion is as if a strong force had dragged the more dorsal parts backward, at the same time pressing down and pushing the lateral part of the neostriatum ventrad over the lateral aspects of the hemispheres.

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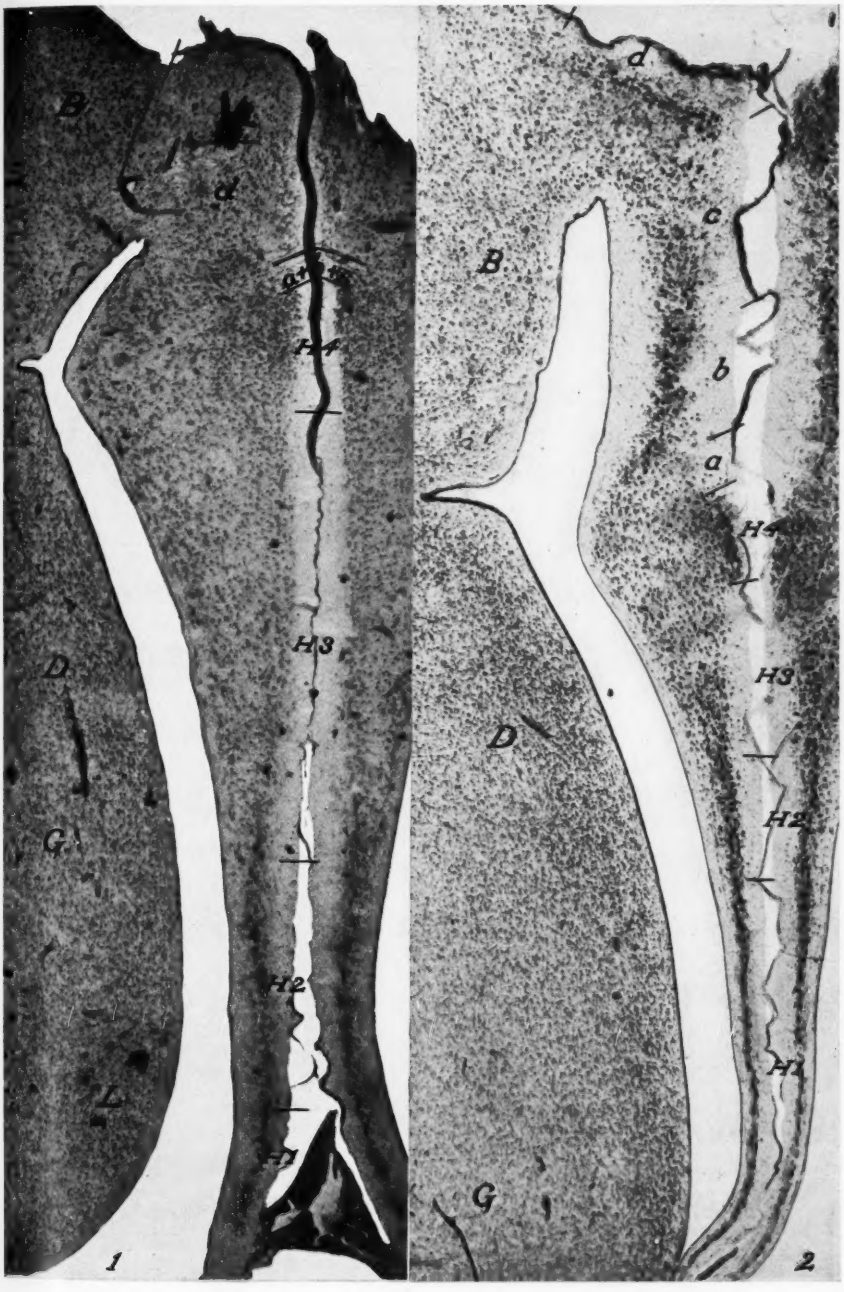

Fig. 1. Fig. 2.

CRAIGIE—THE CEREBRAL HEMISPHERES OF THE KIWI AND EMU

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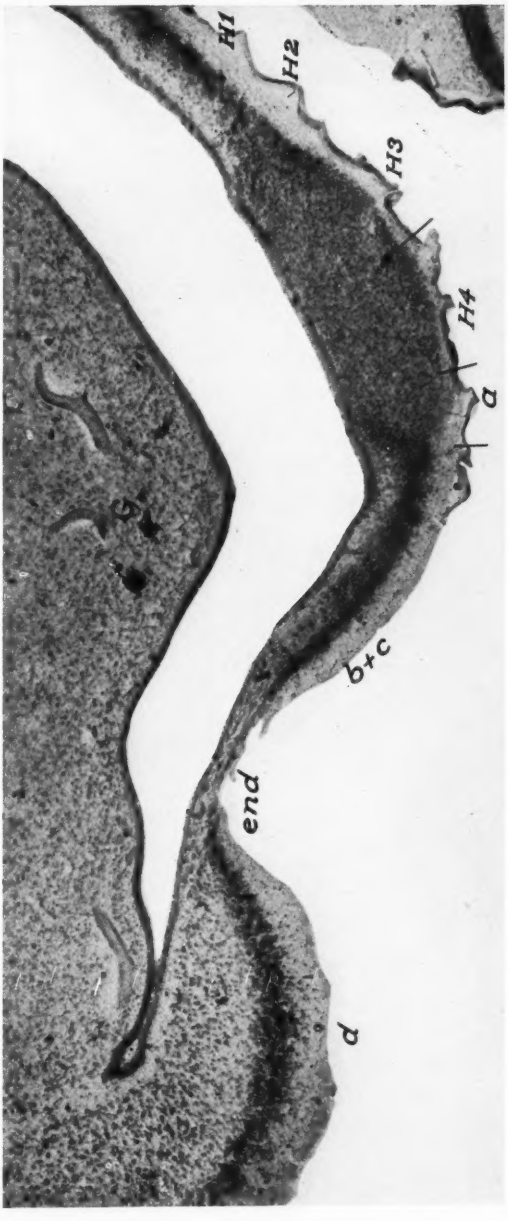

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EXPLANATION OF PLATES I AND II

PLATE I

Fig. 1. Photomicrograph of the medial portion of a transverse section of the left cerebral hemisphere of *Apteryx* about 1 mm. behind the interventricular foramen. Mag. ×24. The plane of the sections of *Apteryx* is indicated in fig. 5 of the 1930 paper. *B*, hyperstriatum accessorium; *C*, *D*, divisions of neostriatum superius; *H* 1, *H* 2, *H* 3, *H* 4, divisions of hippocampal formation; *a*, *b*, *c*, *d*, divisions of parahippocampal pallium.

Fig. 2. Photomicrograph of the medial portion of the cerebral hemisphere of the emu about 2·8 mm. in front of the interventricular foramen. Mag. ×20. Lettering as in fig. 1.

PLATE II

Photomicrograph of the ventral portion of the left cerebral hemisphere of *Apteryx* about 3 mm. behind the interventricular foramen. Mag. ×31½. Lettering as in Plate I, fig. 1 *end*, endoparahippocampal groove.

ANATOMICAL NOTES

COMPLETE ABSENCE OF SEPTUM PELLUCIDUM

By BHUPENDRA NATH BASU, M.B.
Assistant Professor of Anatomy, Carmichael Medical College, Calcutta

THE subject, from whom this specimen was secured, was a Hindu male aged 42 who died of tuberculosis of the lungs without any brain complications. This abnormal condition did not produce in him any defect in the physiological function of the brain.

A horizontal section of the cerebral hemispheres was made from above until the corpus callosum was exposed. The latter was next divided by three incisions and the

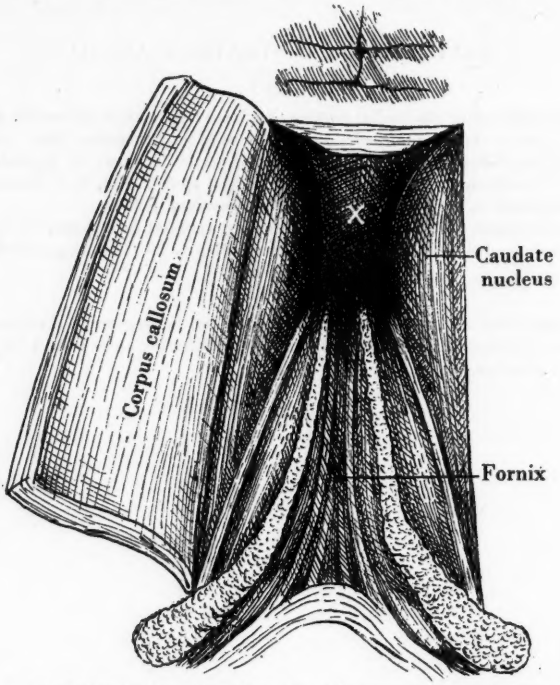

Fig. 1. Dissection to show that there is a wide communication between the two lateral ventricles due to absence of septum pellucidum.

flap was reflected laterally as shown in fig. 1. The anterior horn and the body of the lateral ventricles of the two sides were exposed to view. On examination of the parts in this region it was found that the septum pellucidum was completely absent and no trace of it could be seen either on the columns of the fornix or lining the inner surface of the body, genu, and rostrum of the corpus callosum, so that the medial wall of the anterior horn and that of the body of the lateral ventricles were deficient.

Consequently there was a wide communication between the lateral ventricles of the two sides in that region. The ependymal lining of the lateral ventricles of the two sides were found to be continuous with each other on the under surface of the body, posterior surfaces of the genu and rostrum of the corpus callosum and over the columns of the fornix.

A sagittal section of the entire brain was made as shown in fig. 2 which also shows the complete absence of the septum (black portion marked *X*). All other portions of the rhinencephalon were found to be present in their normal positions.

A coronal section was also made in the region of the head of the caudate nucleus and also clearly showed complete absence of the septum.

In my opinion the condition was due to the small size of the paraterminal bodies and did not extend above up to the primitive corpus callosum. Consequently when the corpus callosum and the fornix stretched forwards and backwards at about the end of the third month of foetal life, the paraterminal bodies did not grow between

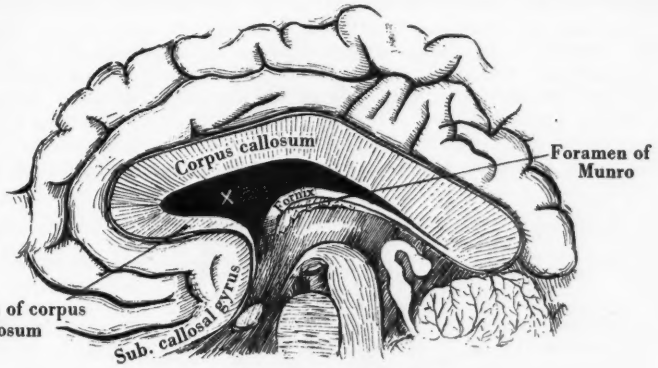

Fig. 2. Sagittal section of brain.

them. Subsequently the mesial surfaces of the two opposite cerebral hemispheres united in the middle line to form the rostrum of the corpus callosum above the upper limit of the paraterminal bodies. Thus on account of the deficiency and failure of growth of the upper part of the paraterminal bodies, the septum pellucidum was not developed at all. Practically the whole of the paraterminal bodies in this case developed into the subcallosal gyrus where the medial tract of the olfactory bulb terminated.

Summary

A case is recorded of:

(1) Complete absence of septum pellucidum in the human brain.

(2) Wide communication between the opposite lateral ventricles.

(3) Continuity of the ependymal lining of the opposite lateral ventricles through this communication.

(4) Small size of the foramen of Munro.

In conclusion I would express my warm thanks to my chief, Prof. M. N. Bose, M.B.C.M. (Edin.), for kindly giving me every facility to review the specimen.

A CASE OF ABNORMALITY IN THE VENOUS SYSTEM OF THE NECK OF THE RABBIT (*LEPUS CUNICULUS* L.)

By G. E. NEWELL, B.Sc.

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It may be of interest to record the following case of abnormality in the venous system of the neck of the rabbit.

From the sketch it will be seen that there is only one anterior vena cava, the right, and that the blood from the left side of the head is brought back to the heart across the

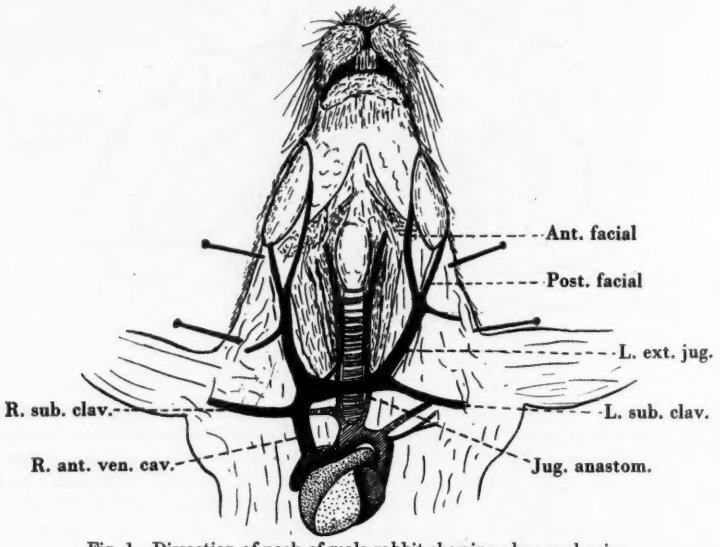

Fig. 1. Dissection of neck of male rabbit showing abnormal veins.

much enlarged jugular anastomosis. In other words, an innominate vein is present. In other respects the venous system is normal.

The interest of this abnormality lies in the fact that the possession of a single anterior vena cava is a normal feature of many Mammals, including Man.

REVIEWS

Anatomy for Dental Students. Systemic and Practical. By Six Teachers. Edited by E. P. STIBBE, F.R.C.S. (London: Edward Arnold & Co.) 1934. Pp. xii + 429, 246 figs. Price 21*s.* net.

For many years those concerned with the teaching of human anatomy to dental students have been awaiting a concise but comprehensive volume which would cover the broad outlines of the subject and include the detailed topographical anatomy of the head and neck, together with instructions for dissecting. Dr Stibbe has produced a book which meets these requirements and which is amply sufficient for the needs of dental students. The subject matter has been selected judiciously, and the descriptions are clear and concise. For the most part the illustrations are excellent—the histology figures remarkably so. It is a pity that the editor has not been so happy as regards terminology. Although he states in the preface that the "nomenclature is the new English version of the Basle nomenclature, with old nomenclature bracketed", perusal of the book fails to confirm the statement. While difficulties are inseparable from the introduction of a new or revised terminology, one cannot help feeling that in this respect the editor has not succeeded in minimising the possibility of confusion.

De Venarum Ostiolis, 1603. *Hieronymus Fabricius of Aquapendente.* Edited by K. J. FRANKLIN, D.M. (London: Baillière, Tindall and Cox.) 1933, pp. 104. 7 figs. and 8 plates. Price 13*s.* 6*d.* net.

The facsimile reproduction of Fabricius's famous work is a welcome addition to the classical library of Medicine and is one upon which both Dr K. J. Franklin and the History of Science Section of the Library of Congress, U.S.A., which has made the publication possible, are to be warmly congratulated. Besides the original text and illustrations—the only change being a reduction in size—we are given a literal English translation both of the text and of the dedicatory epistle to the Illustrious German Nation: a short biographical notice of Fabricius; an account of his famous theatre at Padua and a critical review of the earliest references to the presence of valves in veins.

A study of the work shows Fabricius as a close and accurate observer. He noted, for instance, that the valves were confined to veins, not being found in arteries except in the two large arteries at their origin from the heart; that with few exceptions they were only found in the larger veins of the extremities; that they occurred sometimes as single valves, sometimes in pairs, and that they were particularly found where branches —what we would now call tributaries—arise. His view as to the function of the valves was that they were present to sustain the column of venous blood and thus prevent the blood from stagnating at the extremities of the limbs with a consequent unequal distribution of nutriment—a view which was perhaps the only one possible failing the complete refutation of the current and universally accepted theories on the movements of the blood.

One effect of the publication will be we think to throw Harvey's epoch-making discovery into still bolder relief. The combination of the Editor and the Publications Committee of the Library of Congress has in this instance been such a happy one that we venture to hope it may be continued to the great benefit of all students of medical history.

Features in the Architecture of Physiological Function. By J. Barcroft. (Cambridge University Press.) 1934, pp. x+368, 106 figs., 43 tables. Price 20*s*. net.

It is not often that one sets down a scientific book with a feeling of regret when the last chapter is read. Though the subject matter is always weighty and his argument is close, the book is delightfully written—unconventional, refreshing, provocative of thought and in places humorous.

The philosophy of physiology which the author expounds will be of great interest to anatomists especially to those who are interested in the relation of form to function. Chapters on the internal environment and the rôle it has played in vertebrate evolution, are followed by equally interesting discussions on the storage mechanisms and units of structures and function. The significance of adaptation, duplication of mechanisms and the all-or-none relation are dealt with in a way which removes them from mere academic exercises. The final chapter on the significance of phenomena contains references to problems of sensation which re-open again the old problem of the two-stage recovery of nervous function after nerve section and suture.

Although not a strictly anatomical book, it is one which, as it throws so much light on the present day attitude of physiologists to structural problems, anatomists cannot afford to ignore.

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